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INCEPTION OF SOVIET SYSTEM OF MEDICAL SCREENING OF COSMONAUTS (HOSPITAL STAGE)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 18 Feb 86) pp 3-7

[Article by M. D. Vyadro (deceased) and I. I. Bryanov]

[English abstract from source] The system of medical selection of Soviet cosmonauts stemmed from that used in aviation medicine, particularly medical expertise of flying personnel. Selection in the hospital included two-stage detailed clinical and physiological examinations using various provocative tests. The system of medical selection and clarification of medical requirements was improved and refined through regular observations over candidates and cosmonauts and careful analysis of their grounding due to medical problems. The American and Soviet systems of selection used at an early stage of space programs are compared and similarities and differences between them are indicated.

[Text] Manned flights in space, which were originated by Yu. A. Gagarin, can be considered one of the most outstanding scientific and technological achievements of the second half of the 20th century.

The complexity and range of problems being solved by cosmonauts are increasing from one mission to the next. A moon landing has already been made, and there have been repeated dockings in near-earth orbit of manned and unmanned spacecraft; Soviet orbital stations were developed and are functional; the possibility of man's long-term stay in space (up to 237 days) and performance of a large set of diverse scientific investigations in flight has been proven. People have learned to perform complicated forms of work in open space.

Thus, far, spaceflights have imposed rather high demands on man and his psychophysiological traits. After all, a cosmonaut is not merely an observer-passenger aboard a craft that is controlled automatically. He is primarily an operator who works with complicated apparatus, controls the spacecraft and its systems, conducts numerous investigations under unusual conditions.

After launching space vehicles with animals on board and in anticipation of manned spaceflights, an utterly new, responsible and difficult problem emerged, that of screening individuals who are fit with respect to their health status for missions in space.

The task was set forth in the late 1950's of developing guidelines for the hospital phase of screening cosmonaut candidates and selecting the first groups of cosmonauts.

The difficulties involved in solving this problem were attributable chiefly to the the fact that there was extremely little information at that time about the effects of spaceflight factors on man. It was known that man would be exposed during flights to such factors as accelerations, vibration, noise and weightlessness. However, the accumulated experimental data on the individual effect of some of these factors on man were of relative value, since it was impossible to reproduce on the ground all the factors to which a cosmonaut is exposed during a spaceflight.

Use of a small pressurized cabin advanced the problem of man's exposure to the conditions in a limited closed space in isolation, with considerably altered afferent information, for several days. The data obtained in special anechoic chambers, as well as during long-term high-altitude aircraft flights, were indicative of the possibility of development of special states: illusions, hallucinations, sensations of being "separated" from earth, etc. [6].

Experiments performed with rockets established that a highly organized animal tolerates well the brief exposure to spaceflight factors [4]. However, even these data were of rather limited value to the solution of a wide range of problems referable to the screening problem.

As it undertook development of the hospital stage of medical screening of cosmonauts, aviation medicine had many years of experience in certifying flight personnel referable to different types of aviation, the main elements of which consisted of determining the extent of conformity of somatic, mental and functional reliability of a pilot to the nature of forthcoming professional performance [4, 5].

Unquestionably, this principle had to serve as the basis of the system of cosmonaut screening that was being developed. However, the system of medical certification of pilots could be used for cosmonaut screening purposes only if it were improved with due consideration of the distinctions of cosmonauts' professional activities and conditions under which they occur. This made it necessary to use additional testing methods. They included, in particular, testing on a centrifuge with exposure to high levels of craniocaudal and transverse accelerations, testing on a vibration stand, examination of the vestibular system with use of a new set of methods, more complex set of psychological tests, etc.

It became obvious that healthy, specially trained individuals with high resistance to extreme factors should be assigned to the first spaceflights. With consideration of these requirements, as well as the existence of some elements in common in the professional work of flight personnel and cosmonauts, fighter pilots were to be considered the most suitable candidates for the latter.

It must be noted that, by analogy with the guidelines for expert medical certification of flight personnel, from the very start the screening of cosmonauts was not viewed as a matter of immediate certification, but as a lengthy process

that required constant examination of man under different conditions, including spaceflights. For this reason, a system was developed for screening the future commanders of spacecraft in stages. At first, screening was performed by special visiting commissions to units of fighter aviation, involving pilots 35 years of age or younger, who were deemed fit for flight work without restrictions by medical flight commissions.

In such a multistage system of cosmonaut screening, the hospital stage played an important part, where those screened in the units as candidates were submitted to in-depth clinical and physiological examination using modern methods and special load tests, which made it possible to assess comprehensively the somatic and mental spheres, and functional capacities of the body.

Hospital screening of cosmonaut candidates was performed in two stages. At the first one, there were examinations to the extent provided for certification of fighter pilots. Candidates who completed the first stage of examination with good results were admitted to the second stage, where load tests were used in order to determine resistance to extreme factors.

Candidates who were strictly volunteers and had a distinctly marked purposefulness for their forthcoming work were the main guidelines of screening.

In some cases, candidates who feared a possibility of change in fitness category for flight work refused to go to the hospital for the tests. But, after 12 April 1961, when the mass media began to cover manned spaceflights extensively, there was a psychological change and candidates altered radically their attitude toward the possibility of becoming cosmonauts. This was indicated, in particular, by the numerous letters of pilots who had previously refused to go to the hospital, in which they insistently asked to be called for the examinations.

This psychological change was also attributable to underestimation of the seriousness and difficulty of spaceflights. As a result, some candidates overestimated their capacities, tried to conceal medically unfavorable facts referable to their past and existing deviations of health status.

Some physicians were also subject to such psychological change, and suggested that the requirements as to the health status of cosmonaut candidates be lowered significantly, but this was premature at that time.

Dynamic medical observation of individuals selected for the hospital stage, who were then referred to the Cosmonaut Training Center (CTC) to undergo special and biomedical training, played an important role in improving organizational, methodological and expert aspects of cosmonaut screening.

All of these individuals were essentially healthy. Yet the clinical work-up and tests for tolerance to a set of load tests performed at the hospital established that some candidates presented individual distinctions, both somatic and functional. These distinctions did not serve as an obstacle to special training, but the medical personnel of the CTC concentrated their attention expressly on them: it was assumed that exposure to professional factors during training and spaceflight could have an adverse effect primarily on individuals with the noted distinctions in their health status.

In addition, the results of medical observation could be used as catamnestic data, which permit retrospective evaluation of the validity of the screening system used.

Such tactics were entirely warranted.

First of all, there was a need to revise the attitude toward chronic tonsillitis.

Among the candidates who underwent hospital examination, individuals with this disease were not uncommon. A positive expert decision was made only for candidates suffering from compensated forms of chronic tonsillitis. Further observations revealed that one should adopt a very cautious attitude toward such forms of tonsillitis. Subsequently, a tonsillectomy was required for some cosmonauts, since exposure to the specific training and flight factors was instrumental in exacerbation of tonsillitis, which led to development of a number of pathological reactions and diseases. It is important to mention that, in all cases, the performed tonsillectomy elicited good results.

Some stomatological diseases (dental caries, early stage of periodontosis) also required revision of expert tactics, since they also were subject to exacerbation and complication in the course of special training.

Considering the experience of expert medical certification of flight personnel, no appreciable expert relevance was attributed to moderate dilatation of inguinal rings in the screening of the first group of cosmonauts. However, the results of dynamic medical observation revealed that there was progression of this disease during special training involving intense physical loads in some cases, which sometimes required surgical intervention. For this reason, all candidates in whom these anatomical distinctions were found and who completed the hospital work-up with good results were submitted to surgical management.

Detection of diseases during the period of special training, which served as the cause of disqualification of students and cosmonauts, acquired importance to improvement of the hospital stage of screening. Some of these diseases had not been picked up promptly due to the insufficient range of tests during the in-hospital work-up, while others developed during special training. These data served as grounds for making appropriate additions to the list of mandatory examinations.

Thus, the results of dynamic medical observation of students and cosmonauts during the period of special training and analysis of instances of disqualification for medical reasons made it possible to make the necessary corrections to the system of hospital screening, which were aimed at prompt detection of diseases and distinctions that were potentially hazardous to the professional work of cosmonauts, as well as to define the health requirements for cosmonaut candidates. As a result, the reliability of screening improved considerably.

Some organizational measures were also instrumental in improving the reliability of the entire screening system. In particular, specialists with experience in expert medical examinations began to be called upon for the first, polyclinic stage. The order of the tests was altered at the hospital, and candidates were first examined by specialists in the areas where there was the highest probability of grounding (otolaryngologist, internist, stomatologist). The

numerous labor-intensive laboratory tests were divided into two parts. Those required for diagnostic purposes were performed first within the first days after admission. This saved time and funds.

Implementation of the Soviet program for space exploration made it necessary to include scientists in the spacecraft crew. For this reason, new problems arose concerning screening of cosmonaut-scientists.

First of all, it was important to answer the main question: should all crew members in a multipassenger spacecraft have the same high indicators of health status? It is quite obvious that the answer to this question was determined by the nature of professional work done by each crew member and the need for them to be interchangeable during spaceflights.

Since the duties of scientists during spaceflights were limited to scientific research, it was considered possible to lower somewhat the health requirements. Obviously, one can lower the medical requirements for this category of individuals only if flight factors would not have an adverse effect on their health and would not prevent them from fulfilling the general flight program. However, such an approach could not be extended to applicants for whom performance of research in space was to become their career.

Already at that time, there was reason to believe that the advances in science and technology would gradually broaden the opportunity to allow individuals with some deviations in their health status to participate in spaceflights. But, in view of the need to train professional cosmonauts and to extend the duration of their professional fitness, the requirements as to their health status will remain high for a long time yet. It should be noted that, in the course of implementing the system of cosmonaut screening, data were obtained that enriched aviation medicine and made it possible, in particular, to improve expert medical certification of flight personnel [1, 2].

A comparison of the American system of astronaut screening with the Soviet system used to select the first groups of cosmonauts revealed that they were essentially similar: 1) the cosmonauts were chosen among pilots in both the USSR and United States; 2) cosmonaut screening was performed on the basis of a tested system of pilot screening; 3) the system of cosmonaut screening evolved into an independent scientific direction; 4) both systems involved approximately the same volume of tests to select individuals meeting the highest medical requirements [7-10].

But, in spite of the basic similarity of both screening systems, there were also some differences between them, which pertained to both methodology and organization.

For example, in the United States, much significance was attributed to psychiatric examination with use of a large number of psychological tests; much attention was given to detection of latent diabetes or predisposition for it. There were also differences in methodological procedures of tests used to evaluate the functional state of organs and systems, as well as in modifications of a number of methods.

There were also differences between the two screening systems with regard to approaches to evaluation of professional qualities of candidates: in the United States, a mandatory requirement for the first astronauts was their former occupation as test pilots who had logged many hours on jet aircraft. There were the same high medical requirements for scientist-astronauts as for other crew members [11, 12].

The Soviet system of medical screening, which was used for the first groups of cosmonauts, was subsequently constantly upgraded, with consideration of the accumulated experience in medical support of spaceflights, as well as advances in science and technology.

No doubt, the constant improvement of spacecraft designs will lead to further extension in duration of space missions, expansion and complication of programs of scientific-technical and biomedical investigations which, in turn, will put new tasks to physicians and scientists. For this reason, the importance of the problem of cosmonaut screening will not diminish in the foreseeable future, and consequently there must be constant improvement of the screening system.

A large group was involved in the inception and implementation of the hospital stage of cosmonaut screening: M. D. Vyadro (chief of project), Ye. A. Fedorov, V. M. Tolstov, Ye. T. Malyshkin (internal medicine), I. I. Bryanov, S. R. Raskatova (ear, nose and throat), A. S. Panfilov, Yu. A. Smirnov (neurology), N. S. Ivlev, V. A. Karelin (surgery), V. A. Golubchikov (urology), I. I. Matusevich, Ye. D. Avksentyev (ophthalmology), G. P. Mikhaylovskiy, S. F. Rayev (pressure chamber tests), P. M. Suvorov (centrifuge tests), F. D. Gorbov, K. K. Ioseliani (psychological tests), V. T. Baranov, A. N. Aleksandrov (physiological tests), N. A. Goldin (electrophysiological tests), and R. V. Beleda (clinical laboratory tests).

In those years, A. A. Vishnevskiy and N. S. Molchanov, academicians of the USSR Academy of Medical Sciences, A. N. Babiychuk, doctor of medical sciences, M. M. Filippov and K. F. Borodin were constant consultants in this work; they were of great help in forming the hospital stage of cosmonaut screening, development of requirements as to health status of cosmonauts and interpretation of the obtained data.

The constant close and creative contact with prominent figures in aviation and space medicine--O. G. Gazenko, N. M. Rudnyy, N. N. Gurovskiy, V. G. Terentyev, Ye. M. Yuganov, G. F. Khlebnikov, doctor of medical sciences, A. V. Yeremin, Ye. A. Karpov, as well as many other staff members at the Cosmonaut Training Center, Institute of Biomedical Problems and other institutions--was largely instrumental in the success of this work.

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EFFECT OF SPACEFLIGHT FACTORS ON HEMOPOIESIS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (signed to press 31 Oct 86) pp 7-17

[Article by M. P. Kalandarova]

[English abstract from source] Published data concerning space flight effects upon hemopoiesis are discussed. Possible pathogenetic mechanisms of hemopoietic changes in response to space flight effects are described.

[Text] Hematological studies occupy an important place in the set of methods used to examine individuals exposed to various spaceflight factors. Evaluation of the range of variability of hematological parameters of healthy individuals and determination of the normal range are of paramount importance to proper assessment of the blood system. The norm is a state of equilibrium between an organism and the environment, dynamic conformity of morphological and physiological distinctions to changing ambient conditions [52]. The norm refers to the demarcation limits (top and bottom), within which there may be various quantitative changes that do not lead to qualitative changes in morphological and physiological state of different systems of the body. V. V. Sokolov and I. A. Gribova [61, 62] consider the hematological norm to be the capacity of the blood system to adapt to changing endogenous and exogenous conditions, as a result of which optimum vital functions are provided. The difficulty in interpreting the concept of norm lies in the fact that the variations in normal parameters are wide in different individuals, while the transition from normal to pathology is gradual. Information about the norm is the basis for evaluating the range of adaptability of the body. For hematology, limiting the norm to $X \pm 1.5\sigma$ is the most acceptable, since this means that the normal range is not drastically widened, which is clinically justified, and at the same time such a norm includes parameters encountered in most people (86-95%). With this in mind, in analyzing the hematological data we took fluctuations in the range of $\overline{X} \pm 1.5\sigma$, which are listed in the table, as the norm.

There are heterogeneous data concerning change in erythrocyte count and hemoglobin under the effect of spaceflights and hypokinesia (ground-based experiments): there are indications of both an increase in number of erythrocytes and/or hemoglobin in man and animals [7, 9, 25, 26, 38-43, 55, 56, 64, 66, 72] and a decline of their levels [6, 10, 11, 17, 21, 40, 41, 42, 57, 65, 76, 79, 80, 88, 90, 83, 93, 95, 97]. It was shown in several works [18, 19, 50, 51] that no

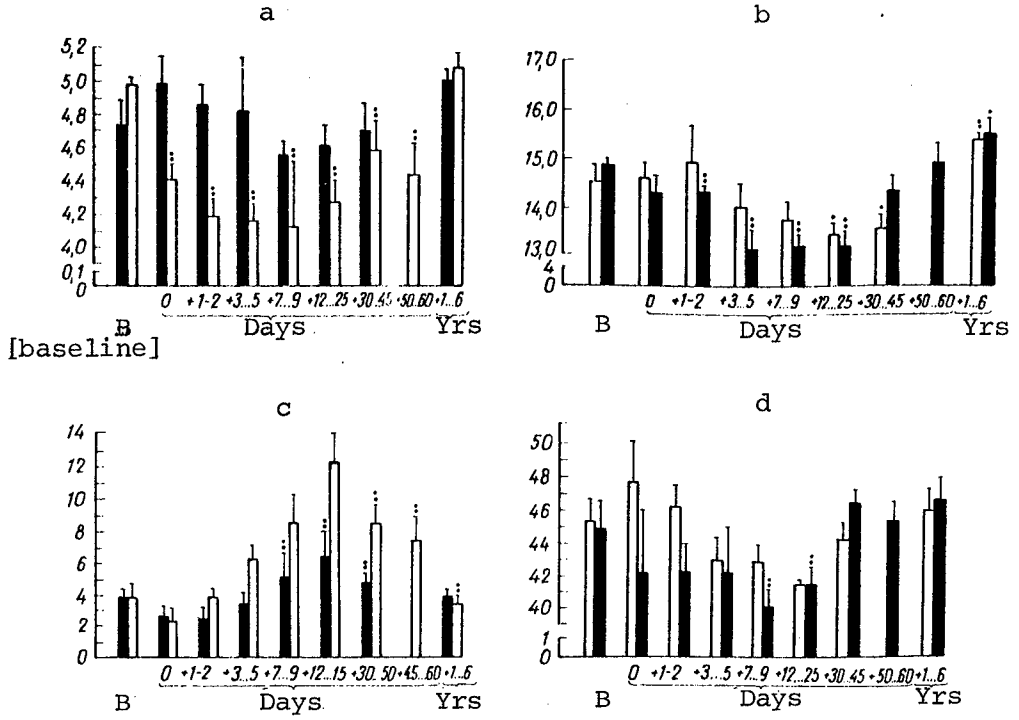
decline in number of red blood cells or dry packed erythrocytes are demonstrable in cosmonauts, as well as animals (dogs), when submitted to postflight tests.

Normal red blood parameters in ordinary men (1) [34, 61, 62] and in male cosmonauts (2) [39, 40]

Parameter	Subject	X	$X \pm 1,5$	X_{min}-X_{max}
Erythrocytes, $\cdot 10^6$	1	4,6	4,0—5,1	—
	2	4,88	—	4,72—5,15
Hemoglobin, g%	1	14,8	13,0—16,5	—
	2	14,8	—	13,37—18,0
Color index	1	0,93	0,82—1,05	—
	2	0,92	—	0,88—0,92
Reticulocytes, ‰	1	7,0	2,0—12,0	—
	2	6,0	—	
Hematocrit, %	1	—	—	40,0—48,0
	2	43,0	—	42,0—48,0
Mean red cell diameter, μm	1	7,5	—	6,7—7,7
	2	7,5	7,3—7,69	—
Osmotic resistance of erythrocytes	1	—	$\frac{0,48}{0,34}$ — $\frac{0,46}{0,32}$	—
	2	$\frac{0,475}{0,338}$	$\frac{0,4699}{0,336}$ — $\frac{0,4801}{0,340}$	—

Note: Minimum values are given in the numerator and maximum, in the denominator.

Thus, according to the data of V. I. Legenkov, hemoglobin rose from 14.4±1.4 to 16.4±1.3 g% in the early hours after landing (missions of up to 18 days) as compared to preflight level in cosmonauts. After long-term (16-175 days) missions, erythrocyte count and hemoglobin differed little from the preflight levels immediately after landing, in most cases, then declined for 1-3 weeks: 16.4% decrease in erythrocytes and 10.5% decrease in hemoglobin. Subsequently, these parameters gradually increased and there was complete or almost complete restoration by the 45th-60th day (see Figure). The results of interferometric examination of dry packed erythrocytes, which were submitted by O. K. Gavrilov et al. [18], indicated that the parameters of dry erythrocytes remained on the level of physiological fluctuations in cosmonauts who had participated in both short- and long-term spaceflights. Thus, after an 8-d flight, the distribution of erythrocytes in cosmonauts as a function of dry mass remained within the control range. After a 140-day mission, there was an increase in number of red cells with low mass on the day of landing and 1 day later, as compared to preflight data. However, the values did not exceed the range of physiological fluctuations. Swisher [104] observes that there is no proof of overt decrease in erythrocyte mass and hemoglobin in astronauts. According to Kimzey et al. [92], erythrocyte preparations made from blood samples taken within 2 h after splashdown from members of the third crew of the Skylab orbital station (84-day mission) were essentially normal according to all standard criteria. The results of microspectrophotometric examination of individual cells revealed that there had been no changes in hemoglobin content. The mean amount of hemoglobin per erythrocyte was also normal.



Dynamic changes in erythrocytes (a), hemoglobin (b), reticulocytes (c) and hematocrit (d) in cosmonauts after spaceflights [42]. Black bars--missions lasting up to 16-18 days; white bars, up to 30-175 days; baseline--preflight data, 0--postlanding day zero, numerals with plus sign--postflight day of test, *n*--number of cases; Dots over bars: one--$P<0.05$, two--$P<0.001$, as compared to baseline

It is necessary to have data concerning the proportion of erythrocytes and plasma (hematocrit parameters) in order to assess the anemic syndrome to rule out hydremia or, on the contrary, thickening of blood ("masks of anemia and erythrocytosis"). After analyzing the hematocrit parameters submitted in different reports [7, 11, 20, 35, 40-43, 66, 77, 88, 96, 97], we arrived at the conclusion that hematocrit fluctuated within the normal range (with a tendency toward decline to the bottom of this range) (see Table) in cosmonauts after 3-175-day missions and astronauts after orbital flights in Gemini, Apollo, Skylab-2 and Skylab-3, as well as tested subjects and animals (dogs, rabbits, rats) submitted to hypodynamia for 18 h to 60 days; the only exception was referable to cosmonauts who flew for 63 days, whose hematocrit dropped to 33.75-38.0% at all tested postflight times (0-45th days) and 26 days before the mission (37.75%).

Some authors interpret the fluctuations of hematocrit, which usually did not exceed 3-10% of the baseline, as a decline and others, as an elevation, while others yet mention the phasic nature of changes in this parameter. The authors drew their conclusions mainly on the basis of comparing the results to baseline data, i.e., data obtained before the flight or experiment, and occasionally to

individual hematological parameters of each subject. With such comparisons, the authors could have estimated the deviation of parameters from mean values at a time preceding the flight or hypokinesia in either direction, and could even prove the reliability of these changes under the influence of a concrete factor. However, in order to assess the nature of quantitative changes demonstrated in such a comparison, it is necessary to compare them to the conventional norm. Most people present deviations to one side or other of mean parameters. In real life, body functions are provided by broad fluctuations of morphological and functional parameters, which concentrate near the mean level. It is not a single mean value, but a certain range of deviations from the mean due to some individual distinctions or influence of the environment that best corresponds to the conception of norm. If we compare the range of fluctuations of hematocrit, erythrocytes and hemoglobin in the above-described studies (this is particularly graphic in the Figure) and compare them to the norm and parameters of cosmonauts (see Table), it becomes understandable that the fluctuations of these parameters do not exceed the range of normal values; however, they were lower than the base values for the cosmonauts.

Thus, on the basis of analysis of the results of hematological tests following spaceflights lasting up to 175 days, as well as on subjects during exposure to hypokinetic conditions and in the recovery period after it, we concluded that with exposure to the above factors there is a decline in erythrocyte count and hemoglobin to values that are close to the bottom of the normal range and, in isolated cases, below it [17, 41].

In this survey, we are expressing our opinion concerning the genesis of the above changes in the erythron under the effect of spaceflight factors and hypokinesia.

The decline in erythrocyte count and hemoglobin could occur due to loss of blood (posthemorrhagic), increased breakdown of blood (hemolysis) or impairment of hemopoiesis (hyporegeneration). No evidence of loss of blood was obtained in the studies of Soviet and American scientists [38, 40, 97].

Testing of feces for occult bleeding was always negative, and there was no change in fraction composition of bilirubin. Nor is there any evidence of hemolysis. Thus, data are submitted which indicate that the erythrocytes had a normal life span--120 days with a range of 113 to 130 days--in astronauts (Gemini flight) and during hypokinesia (35-day bedrest) [10, 89, 97, 98, 106].

The reticulocyte reaction (overt reticulocytosis) was demonstrated 1-3 weeks after long-term flights, and occasionally the reticulocyte count was 5-7 times higher than the preflight level, although mean reticulocyte level did not exceed the range of physiological fluctuations [41] in such cases, as well as in the 3d week of the recovery period following hypokinesia [97], as can be seen in the figure and table.

As for dynamics of reticulocyte content during a spaceflight and on the 1st day after, we can mention a tendency toward decline by a mean of 33% in this parameter as compared to the baseline [38, 40-42, 83, 95].

No reticulocytopenia was demonstrable, although there was a tendency toward decrease in reticulocytes even with hypokinesia [7, 43, 44, 55, 57, 72, 97].

In order to evaluate the general picture and pathogenesis of red blood changes one must have an idea about the size of erythrocytes. V. I. Legenkov et al. [40, 42] and Ye. I. Vorobyev et al. [13] observed a tendency toward microcytosis of erythrocytes in cosmonauts following missions lasting 63 or more days. The peak of the Price-Jones curve was in the range of 5.4-6.1 μm after landing. The mean diameter of erythrocytes was 6.1 μm in the second crew of Salyut-4 in the 1st week after the mission (7.5 μm preflight). In hematology, it is considered that erythrocytes with a diameter of less than 6.7 μm are referable to microcytes and those with a diameter of over 7.7, to macrocytes.

The mean thickness of erythrocytes, which was 1.9 μm on the 7th postflight day (normal 1.9-2.1 μm) and 2.1 sphericity index (under 3.4 indicates a tendency toward spherocytosis) are also indicative of microcytosis at this time in the cosmonauts.

Since the color index was normal, one should believe that the microcytes were normochromic. Microspherocytosis of erythrocytes in the 1st postflight week may be indicative of the fact that some of the erythrocytes have an older shape.

However, at certain periods (5th and 12th days following 16- and 30-day flights, respectively), the mean diameter of cosmonauts' erythrocytes was larger (8.2 μm) than before the flight (7.5 μm). Some astronauts also presented an increase in mean diameter of erythrocytes, but immediately after the flight [90, 91, 96, 106]. At the same time, according to the data of Kimzey et al. [92], there were no overt changes in size or shape of erythrocytes in members of the third crew of Skylab immediately after the mission (2 h after splashdown), as compared to preflight values. The red blood cells were essentially normochromic. Consequently, microcytosis and macronormocytosis were observed postflight in the cosmonauts.

There is some relationship between the shape of erythrocytes and their resistance to hypotonic solutions. Spherocytosis should be viewed as the first, preparatory stage of hemolysis. Reticulocytes, which are "macroplanocytes," are more resistant to hypotonic solutions than old, worn-out erythrocytes that are closer to microspherocytes in shape. The nature of erythrocyte aging is related in essence to the surface membrane: changes in its configuration and composition [8]. The data in the literature concerning change in osmotic resistance of red blood cells following spaceflights and hypokinesia are rather contradictory. The material reported by V. I. Legenkov et al. [41] indicates that both minimum and maximum osmotic resistance of erythrocytes fluctuated in the cosmonauts essentially within the normal range, although in some cases there was a tendency toward decline.

There are reports of some decline of osmotic resistance of erythrocytes following spaceflights [60, 76, 92, 99], as well as either no changes [7, 43] or a decline [57, 65] in resistance of erythrocytes to hypotonic NaCl solution under hypokinetic conditions. The tendency toward microspherocytosis and decrease in osmotic resistance of erythrocytes, which is indicative of relative increase in share of old erythrocytes, as well as minor decrease in number of reticulocytes and erythrocytes (as compared to the baseline), which were demonstrated in a number of cosmonauts, may be indicative of some decrease in physiological regeneration of red cell precursors during spaceflights. This is confirmed by the results of hematological studies obtained by a number of researchers [73, 75,

76], including us, in an experiment aboard Cosmos-605, which indicate that there was some decline in physiological regeneration of hemopoiesis in rats, mainly due to decreased erythropoiesis. It was suggested by Yu. I. Grinshteyn and N. N. Skachkova [22] that the decrease in lipoproteins of red blood cells leads to structural alteration of the membrane and change in permeability for sodium ions, as a result of which there is change in the shape of the red cell, its deformability and premature hemolysis occurs.

Hyporegeneration of erythrocytopoiesis, in the development of which iron and erythropoietin play an important part, can lead to anemia. Astronauts who performed the Apollo program presented a moderate decrease in transferrin, and the crew of Skylab showed a change in rate of iron turnover [87]. Tavassoli [105, 106], who analyzed data in the literature concerning the causes of decreased erythrocyte mass in astronauts, believes that development of iron-deficient states during spaceflights is unlikely. He indicates (referring to the data in [92, 94]) that iron and transferrin content in serum of astronauts was normal.

Several Soviet cosmonauts who participated in missions lasting 145-175 days were found to have a tendency toward decrease in serum iron, general iron-binding capacity of serum and unsaturated serum capacity, as well as decrease in iron concentration of hemoglobin on the 1st and 8th days after landing and, in some cases on the 14th day [24]. At the same time, serum ferritin content was normal after 175-185-day missions.

A. P. Andreyeva et al. [4] reported low iron levels in cosmonauts after a 96-day flight. Lancaster [97] mentioned a decrease in plasma iron content during bed-rest (35 days). V. M. Gordiyenko [21] observed significant (3-10-fold) drop of bone iron level on the 240th-360th days of immobilization. The opinion is held [111] that most of the iron going to hemoglobin is taken from the bone marrow stroma, and for this reason the results obtained by V. M. Gordiyenko [21] merit attention. He also found a decrease in levels of other trace elements in bone: manganese, copper and aluminum.

It is known that if there is a low iron content, a latent iron deficiency may develop--siderocytopenia without anemia. This stage of iron deficiency can be manifested by an increase in microcytes and appearance of anisocytosis [30, 34, 53, 58, 59, 85]. The tendency toward microcytosis and anisocytosis demonstrated by V. I. Legenkov et al. [41] in cosmonauts, as well as by V. M. Gordiyenko [21] and other authors in relation to hypokinesia, could be due, to some extent, to a latent iron deficiency. It should be noted that formation of erythropoietins can be limited not only by genuine depletion of iron, which is encountered in iron-deficient states, but by its redistribution due to impaired release from reticuloendothelial cells into plasma. In such cases, when the total iron content of the body is unknown, there is an increase in reserve, decrease in level of transport iron followed by its insufficient passage into bone marrow for erythrocytopoiesis. Defective release of iron into plasma has been noted in the presence of chronic and acute infectious-inflammatory processes.

There are data in the literature [19, 21, 38, 40, 63, 70] concerning a decrease in resistance to infections during spaceflights and in experiments with hypo-kinesia, as well as in clinical practice when the limbs are immobilized. Some toxic and toxic-allergic factors play a part in onset of iron deficiency [1, 68].

According to Yu. G. Nefedov et al. [48], S. N. Zologuyev and M. M. Shinkareva [29], Ye. I. Vorobyev et al. [15, 16] and a few others, during spaceflights there is increase in level of microorganisms (staphylococci, streptococci and others) in the upper respiratory tract and on the cosmonauts' integument. In spite of the increased amount of autogenic microflora, no inflight infectious diseases have been recorded. Aside from disturbances in iron metabolism, erythropoietins play a rather important role in the genesis of insufficient production of hemoglobin and red blood cells, in particular, in the presence of chronic infection [54, 82]. The studies of V. I. Legenkov et al. [41, 42] and V. I. Gudim et al. [23] revealed that erythropoietin level was elevated in cosmonauts for a month after landing. In most cosmonauts who had flown for more than 2 months, serum erythropoietin level was lower than in those who had spent a shorter time in space (up to 1 month).

A decline of blood erythropoietin had been observed in hypodynamic people [43-45, 47, 77, 88, 97]. The cause of long-term elevation of erythropoietin in cosmonauts following short-term missions (up to 1 month) is unclear.

The committed stem cell population of bone marrow is the target cell of both erythropoietin and iron. Stimulation of cells that are precursors of erythropoiesis by erythropoietin, provided there is adequate access of iron for hemoglobin synthesis, is a deciding factor for maintaining normal blood composition.

The most likely cause of excessive erythropoietin in cosmonauts after missions is apparently its nonuse due to some decline of physiological regeneration in flight, as indirectly indicated by the decrease (in relative and absolute terms) in erythroblast elements in rats on the 1st-2d day following a 22-day spaceflight [32]. According to V. N. Shvets [75], inhibition of erythropoiesis in animals submitted to 3-week spaceflights (experiments aboard Cosmos-60, Cosmos-782 and Cosmos-936 biosatellite experiments) is related to decrease in number and proliferative activity of CFU (colony-forming units). In particular, the absolute number of bone marrow CFU in the humerus of flight group rats (Cosmos-936) fell to 1/18-1/21 as compared to the control, 1-2 days after landing.

A number of researchers have demonstrated diminished erythropoiesis in hypodynamic rats, mice and dogs [9, 43, 55, 71-74, 81].

According to this analysis of the literature, the decrease in number of reticulocytes, erythrocytes and hemoglobin to levels that are close to the bottom of the normal range and, in a number of instances, below it, and the reduction in volume and diameter of erythrocytes in some cosmonauts and hypokinetic subjects are attributable to hyporegeneration of erythropoiesis. Decrease in differentiation of stem cells into the erythroblast and, perhaps, iron deficiency and incomplete utilization of erythropoietin play an important part in the genesis of hyporegeneration.

Inhibition of erythropoiesis during spaceflights in the course of physiological regeneration of bone marrow could be due to the body's lower erythrocyte requirement in weightlessness as a result of limited motor activity [37, 42].

It is known [36] that there is a correlation between extent of development of erythron and muscles. Athletic conditioning stimulates development of the

muscular system and is instrumental in increasing erythrocyte content. Physiological functions depend on the distinctions of current function and level of development of skeletal muscles [5]. An increase in relative mass of erythrocytes in ontogenesis is related to systematically increasing motor activity of skeletal muscles, which leads to progressive increase in hemopoiesis with increase in muscle mass. There is information to the effect that there is a greater mass of blood, higher erythrocyte content in individuals with an athletic constitution than in those with poor muscular development. This is no doubt an important argument for explaining the decline of physiological regeneration of erythropoiesis during spaceflights and hypokinesia, when noticeable reduction of muscle mass is observed, but apparently it is not the only one. There may be other causes, to which attention must be paid and which must be explored. In particular, we cannot rule out development of reciprocal relations between primordical elements of bone marrow, manifested by the fact that, along with increase in number of cells of one class (apparently due to stimulation) there is decrease in number of cells of other classes, which were apparently not stimulated. We are alerted by the fact that V. N. Shvets [75, 76] observed not only a low concentration of CFU, but that there was appearance of primarily granulocyte colonies in recipient bone marrow (72.7% versus 28.0% in the control), after transplantation of bone marrow taken soon after the flight, while the number of erythroid colonies dropped to 13.6% (51.5% in the control) in rat bone marrow, on the 1st-2d day after the experimental flight (Cosmos-936). He observed inhibition of erythropoiesis, while the number of granulocytic elements increased by about 32 times, as compared to the level of these cells in a group of control animals. Consequently, in rats there is marked decrease in capabilities in the direction of erythropoiesis, while granulocytopoietic capabilities increase significantly, which is consistent with the results of examining dividing and maturing pools of bone marrow cells from these rats. According to current conceptions, the microenvironment plays a major role in differentiation of hemopoietic stem cells [27, 49, 67, 69, 105, 106, 109, 110]. In particular, it was reported [49] that there is a change in erythropoietin-stimulating action of erythrocytic factors with blocking of macrophage cells of the bone marrow stroma (system of mononuclear phagocytes). It is assumed by the cited author that there may be formation of substances similar in effect to erythropoietin in the zone of the hemopoietic microenvironment, and macrophage cells are probably responsible for this process. The system of mononuclear phagocytes is the main defense system. Macrophages are also responsible for production of colony-stimulating factor that controls granulocytopoiesis and for "providing" iron to erythroid elements [108]. Functional insufficiency of the monocyte-macrophage system may develop under the effect of endogenous factors.

Tavassoli [105, 106] believes, not without justification, that spaceflight factors have a stronger influence on bone marrow stroma than on hemopoietic stem cells. In his opinion, restoration of stroma when there is a low rate of cell turnover requires more time than is needed for restoration of hemopoietic stem cells (with high rate of cell turnover). A. Ya. Fridenshteyn and Ye. A. Luriya assume that there is slow elimination of a defect in the microenvironment, or none at all. The capacity for regeneration of stromal stem elements is considerably lower than that of hemopoietic stem cells. However, we cannot rule out disturbances in pools of stem or committed cells, which may occur due to change in their sensitivity to normal regulators of hemopoiesis, for example,

following infections [100]. This could also explain, to some extent, the rise in hemopoietin levels in blood of cosmonauts following spaceflgihts.

Since there is a close link between bone tissue and bone marrow, it is logical to assume that the decline of erythropoiesis in weightlessness could be largely attributable to destructive processes in bones (atrophic changes, osteoporosis, decrease in Ca content and trace elements) [14, 13, 21, 103]. Tavassoli [106] suggests that destruction of bone and depression of erythropoiesis be viewed as parallel processes. Depression of erythropoiesis in weightlessness may not be related to impaired osteogenesis in rats, at least for the first 3 weeks of a spaceflight [75]. Another aspect of the problem must be discussed. A distinction must be made between the process on which bone marrow regeneration is based during a spaceflight and with restriction of motor activity in general: bone marrow hypoplasia or physiological decline of hemopoiesis (partial erythrocytopoiesis). This is one of the problems encountered in studying hemopoietic disturbances in weightlessness and with hypokinesia. These are two basically different processes with regard to their course, although both are based on hyporegeneration, which is usually irreversible in the former case (adverse prognosis) and reversible in the latter (favorable prognosis).

The hypothesis has been expounded that aplasia of hemopoietic organs may develop in weightlessness [37, 89, 101]. In the opinion of Swicher [104], V. I. Legenkov and Yu. N. Tokarev [40, 42], bone marrow function diminishes in weightlessness, since there is no need for activity to remain the same as in normal gravity. There are grounds to believe that expressly the decline in functional activity of hemopoiesis (primarily erythropoiesis) is the prime factor in the genesis of the blood changes observed in cosmonauts following spaceflights and with hypokinesia. Integrity of granulocytopoiesis with marked leukophil and neutrophil reaction in blood and restoration of morphological composition of blood (including erythrocytes) some time after exposure to flight factors or hypokinesia indicates that this reaction is physiological (adaptive).

Deafferentation is considered one of the possible causes of onset of the anemic syndrome during spaceflights [28]. The higher branches of the central nervous system are involved in controlling the erythrocyte part of the blood system [12, 31, 33]. In the presence of neurogenic anemia, there may be "inhibition" of differentiation and maturation of bone marrow cells.

However, we cannot entirely rule out hypoplasia, in the development of which such factors as an adverse microenvironment, immunologically mediated destruction of precursor cells, absence of regulatory hormones and inducing substances may be involved [78].

Combined hematological programs are needed to assess the compensatory capacities of the blood system, which should include investigation of bone marrow function (including immunology of stem cells, stromal elements, kinetics of proliferation, differentiation and maturation processes), study of correlation between bone and hemopoietic tissues, investigation of cellular (interaction of T lymphocytes and monocytes) and humoral regulators of hemopoiesis, vitamins (particularly C and B_{12}), erythropoietins and trace elements. To rule out iron-deficient anemia, one should pay attention to dynamic analysis of thin, well-stained blood smears, reticulocyte content, amount of iron and ferritin in serum, iron-binding capacity

of serum and sideroblasts in bone marrow. Life span of erythrocytes, as determined by means of labeled Cr and stercobilin assay in feces will permit evaluation of presence and extent of hemolysis. Such mechanisms as primary defect of stem cells, microenvironment, presence of circulating antibodies against precursor cells of different lines of hemopoiesis and suppressor nature of T lymphocytes may be considered in the pathogenesis of aplastic anemia.

A mandatory condition for determination of the nature of anemia and investigation of its pathogenesis is to rule out contact with additional, anemia-provoking factors, such as infections, drug intake, which lead to iron deficiency, allergic reactions with formation of autoantibodies that cause depression of bone marrow hemopoiesis [2, 3, 46, 84, 102].

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 613.693-07:612.822-056.17-087

EVALUATION OF FUNCTIONAL STATE OF PILOTS ON THE BASIS OF INTERHEMISPHERIC ASYMMETRY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 23 Sep 85) pp 18-21

[Article by V. A. Bodrov and A. G. Fedoruk]

[English abstract from source] The stability of the functional asymmetry of brain hemispheres (with respect to the right ear coefficient--REC) of pilots was investigated during their exposure to extreme flight factors. It was found that the functional asymmetry of brain hemispheres was sufficiently stable in the subjects whose initial REC was not less than 10%. After exposure the decline of the REC in some subjects was accompanied by deterioration of their health status and quality of their operational work.

[Text] The problem of functional asymmetry of the cerebral hemisphere is of interest to specialists in industrial physiology and psychology because of the facts accumulated to date concerning the role of interhemispheric relations in transfer and retention of traces of instruction, emotional stability, man's adaptation to environmental conditions, etc. [1, 2, 5, 7, 8, 16, 13, 15].

Some authors report that marked functional asymmetry of the cerebral hemispheres enhances significantly man's capacity for fuller and more precise reflection of the environment, and it is instrumental in formation of adaptation mechanisms [2, 4, 5]. Several investigations revealed the distinctions referable to dynamics and extent of functional asymmetry in the right and left hemispheres when an individual moves to different climate zones, and the link between these parameters and emotional stability and productivity of work [5, 7, 8]. Investigation of the effects of flight factors on asymmetry of blood pressure, skin temperature and certain other autonomic parameters for the right and left half of the pilot's body after performing flights led to the assumption that there is a change in dominant correlations between the hemispheres under different conditions [3]. However, there is no discussion in the literature of stability of parameters of functional asymmetry of the cerebral hemispheres as related to exposure to extreme flight factors and a pilot's working conditions, as well as of the possibility of using these parameters to assess and predict a pilot's functional state.

Methods

At the first stage of these studies, to answer the above questions, we determined the standards for levels of functional asymmetry of cerebral hemispheres (according to right ear coefficient--REC) on 438 pilots and cadets. We used the percentile statistical method used in medical studies for elaboration of anthropometric, somatometric and other standards [11]. We also tested the stability of parameters of functional hemispheric asymmetry according to speech in students and pilots differing in level of professional training. In order to determine the extent of dominance of hemispheres, we used the method of dichotic listening to verbal information [6, 12, 13, 14].

At the second stage, we tested stability of hemisphere dominance according to speech of pilots exposed to some extreme flight factors: radial accelerations of 3-5 G for 30 s at a time, generated on a centrifuge (53 pilots were tested); continuous cumulative exposure to Coriolis accelerations (CCCA). A total of 15 subjects were tested.

The effect of combined flight factors on parameters of functional hemispheric asymmetry was tested by the method of simulation of the conditions of a 6-h flight. The acting factor was hypoxia, corresponding to an altitude of 3500 m, as well as noise of 100 dB and continuous operator work. The quality of performance of operator work (two-dimensional compensatory tracking and solving arithmetic and logic problems at a forced pace) was determined according to time parameters and number of mistakes made. The functional state of operators was evaluated on the basis of changes in parameters of heart rate, respiration rate, minute volume and the SAN method (wellbeing, activity, affect). A total of nine operators participated in these tests. A series of flight tests was conducted, in which 32 pilots participated, in order to confirm the results of laboratory tests. A total of 88 flight tests were performed.

Analysis was made of functional asymmetry of cerebral hemispheres according to speech of pilots and operators differing in tolerance to factors used, as well as in relation to the quality of their professional performance, in order to determine whether it is possible to use parameters of functional asymmetry of cerebral hemispheres to assess and predict functional states. Tolerance to flight factors was evaluated by methods that are used for expert medical certification of flight personnel [10].

Results and Discussion

The results obtained at the first stage enabled us to define the standards for parameters of functional hemispheric asymmetry (according to value for REC). It was established that REC values of 2-5% are very low, 6-10% are low, 11-25% are below average, 26-40% are average, 41-50% are above average, 51-65% are high and over 65% are very high.

In order to determine the degree of functional hemispheric asymmetry in flight personnel during advancement of their professional training, we analyzed REC for 1st-4th year cadets and pilots with different qualifications. We found that REC values were rather stable between the level of training of a 1st-year cadet to pilot second class, constituting 17.2±3.6% in cadets to 25.0±8.0% in pilots ($P>0.05$). The only exception was referable to pilots with the highest level

of professional training. For this group of pilots, the mean REC was 41.1±2.5% ($P<0.001$). With respect to this fact, the hypothesis can be expounded that there is gradual increase in lateralization of hemispheric functions in the course of formation of high professional skill and during long-term performance of complicated types of flights. In addition, it is also possible that primarily pilots with pronounced parameters of functional asymmetry achieve the highest level of professional training in such a difficult form of work. The data of other authors concerning low REC in individuals in other occupations may serve as confirmation of this statement [6].

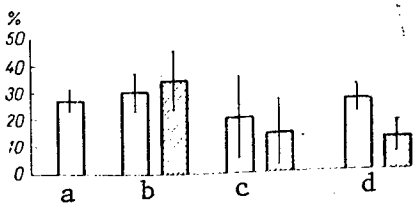

Figure 1.
Changes in parameters of functional hemispheric asymmetry (%) under the effect of accelerations. White bars--before exposure, striped--after
a) control
b) pilots who tolerated exposure well
c) pilots who tolerated it poorly
d) exposure to CCCA

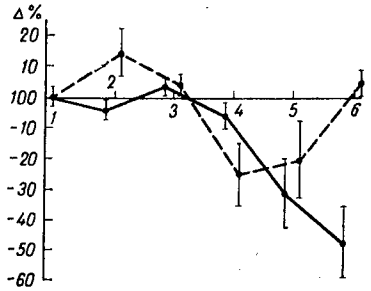

Figure 2.
Dynamic of parameters of interhemispheric asymmetry and quality of operator performance under conditions simulating 6-h flight.
Boldface line--REC, dash line--quality of performance; x-axis, work time, h

As a result of the second stage of our studies, it was established that exposure to radial accelerations had no appreciable effect on REC of pilots (Figure 1b, c) However, some distinctions were demonstrable: REC has a tendency toward rising in pilots who tolerated accelerations well and toward declining in those who tolerated this factor satisfactorily. We also observed that the baseline REC was 11% higher in pilots with good tolerance to accelerations than in those with satisfactory tolerance. It is known that, in addition to radial accelerations, Coriolis accelerations have an appreciable effect on pilots [9]. For this reason, we tested REC values before and after exposure to the latter. The obtained results are illustrated in Figure 1d.

As we see, there is decline to less than 1/2 in REC after exposure (from 25.9±5.5 to 12.5±2.7%; $P<0.05$). In all cases where this factor was used, we observed worsening of the subjects' wellbeing with autonomic manifestations.

During performance of professional duties for 6 h continuously with exposure to hypoxia and noise, a decline of REC was observed after 3-4 h of work (Figure 2). By the 6th h of work it decreased to 40% of the baseline ($P<0.001$). After working for 3 h, the operators also presented a progressive sensation of fatigue, appearance of pain in dorsal muscles and heaviness of the head. These subjective signs persisted to the end of the study and were associated with changes in physiological parameters indicative of development of marked fatigue.

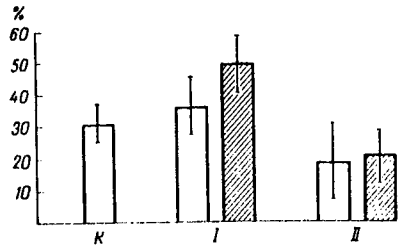

Figure 3.
Parameters of interhemispheric asymmetry (%) in pilots whose flight assignments were rated as good (I) and satisfactory (II). White bars--preflight, striped--postflight; K--control

This study also revealed worsening of operator performance. According to the data illustrated in Figure 2, the quality of operator performance, in particular, performance of motor-logic problems within a limited time, diminished by an average of 20% after 3 h of continuous work, as compared to the baseline ($P<0.05$).

The data obtained under laboratory conditions were confirmed in the flight test (Figure 3). After 2-3 flights, regardless of quality of performance of flight assignments, the pilots' REC rose by a mean of 7% ($P>0.05$). It must be noted that there were differences in extent of REC increase (as compared to the baseline) in pilots whose performance was given different ratings. REC increased by 13.1% in pilots whose flight assignment was rated at least as good, and it increased by only 1.8% ($P<0.001$) in those with lower ratings. We were also impressed by the fact that baseline REC was 16.8% higher in the former group of pilots than in the latter. These findings are consistent with the data obtained from testing stability of REC in pilots exposed to accelerations. This fact may indicate that marked lateralization of hemispheric functions causes higher tolerance to flight factors, and is also instrumental in better performance of professional duties.

Thus, investigation of dynamics of parameters of functional asymmetry of the cerebral hemispheres during professional training of pilots, as well as exposure to different flight factors and combinations thereof, enabled us to establish the following: 1) with high tolerance to the factor used, REC has a tendency toward increase and with low tolerance, on the contrary, toward decrease; 2) its baseline value is also important: the higher it is (mean normal value of at least 10%), the better the tolerance to flight factors; 3) the extent of hemispheric asymmetry is related to the functional state of the pilot or operator, as well as quality of their professional work. The obtained facts can be used in screening flight personnel, evaluating and predicting their functional state.

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INDIVIDUAL DISTINCTIONS OF FLUID-ELECTROLYTE METABOLISM DURING HYPOKINESIA WITH HEAD-DOWN TILT FOR 120 DAYS, AND EFFICACY OF PREVENTIVE AGENTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 7 Jan 86) pp 21-24

[Article by T. M. Smirnova, G. I. Kozyrevskaya, V. I. Lobachik, V. V. Zhidkov and S. V. Abrosimov]

[English abstract from source] Sodium balance and circulating plasma, intracellular, extracellular and interstitial fluid volumes were measured in the test subjects exposed for 120 days to head-down tilt at -5°. The large scatter of the above parameters was associated with individual variations and with the use of different countermeasures against demineralization (exercise and drugs--xydiphone and glucamak). The effect of the countermeasures was different in both qualitative and quantitative terms. It appears that the target of their action was different. The best prophylactic effect was seen when exercise and drugs were used in combination. These findings suggest that individual variations of fluid-electrolyte metabolism during prolonged hypokinesia are related to the different capacity of tissues for water and electrolytes.

[Text] The dissimilar changes in volumes of body fluids of cosmonauts who participated in flights aboard Salyut [1, 4, 6] and Skylab [9] orbital stations indicate that the methods of correcting fluid-electrolyte metabolism intended for long-term spaceflights must be individualized to a significant extent. In order to elaborate individualized prevention schedules, we studied Na balance and distribution of fluid in the human body during long-term hypokinesia with head-down tilt (HDT) without any preventive measures, as well as with intake of pharmacological agents (PA) and exercise (EX).

Methods

We studied 15 health men 24 to 40 years of age, who maintained bedrest for 120 days with the head end of the bed tilted down to an angle of -5°. Four of them took PA (1st group), 4 (2d group) exercised, 4 (3d group) combined exercise with intake of PA and 3 (4th group) did not use any preventive agents. The set of drugs included agents aimed at preventing changes in mineral metabolism (xydiphone, glucamak), correcting lipid metabolism and pancreatic function

(solism, F-99) and stimulation of hemopoiesis (folicobalamin). The program of pharmacological prophylaxis was developed by B. V. Morukov and E. A. Yuryeva. The set of exercises developed by I. B. Kozlovskaya and A. V. Ovsyannikov was aimed at preventing impairment of skeletomuscular system functions, and it consisted of four modes: high-speed, forced, rapid-forced and passive-active extension of gravity muscle groups. The 1st and 3d groups of subjects underwent a course of ultraviolet irradiation by the program of N. Ye. Panferova et al., in order to replace the shortage of transport form of vitamin D.

HDT was preceded by a 32-day baseline period, during which balance studies were made, as well as determination of body fluid volumes. The diet was the same in the background period and during HDT.

Urine was collected daily, as well as all feces for every 4-day period. Mineral composition of feces and diet was analyzed by standard methods. A previously described method was used to determine mineral composition of sweat [5].

Total fluid volume (TFV) was measured with dilutions in tritium oxide using a Mark-3C liquid scintillation counter; extracellular fluid volume (ECFV) was determined according to dilution of stable Br, the concentration of which in plasma was measured by the roentgenofluorescence method. ECFV was calculated using the formula given in [2]: ECFV = 0.86·A/C, where A is the amount of bromid given per os (in g) and C is concentration of plasma Br (g/ℓ); 0.86 is the coefficient that takes into consideration BR incorporation in erythrocytes and cells of the intestinal mucosa, as well as its level in protein plasma.

Circulating plasma volume (CPV) was measured using ^{131}I-labeled serum albumin, intracellular (ICFV) and interstitial (IFV) fluid volumes were determined by calculations: ICFV = TFV - ECFV; IFV = ECFV - CPV. Fluid volumes were measured 3 days before and on the 60th and 120th days of HDT. To assure comparability of data obtained in subjects of different weight and with different baseline distribution of fluid in the body, all volumes were scaled to relative values, as percentage of individual baseline levels. Reliability of intergroup differences in all parameters was assessed using Student's criterion.

Results and Discussion

In the course of the study we demonstrated changes in Na balance in different directions. It was negative in 10 subjects (2 in the 4th group and all 8 in the 2d and 3d groups). In these subjects, intracellular fluid volume was low by the end of the study, with the exception of 1 subject in the 3d group. All subjects in the 1st group and only 1 in the 4th had a positive Na balance; ICFV was higher than the baseline. ECFV was equally diminished in subjects with positive and negative Na balance (Table 1).

Table 2 lists values for Na balance and changes in fluid volumes as related to different regimens (1st-3d groups). The most marked differences are demonstrable in such parameters as Na balance and ICFV. They were both elevated in the 1st group, as compared to the 4th, and in the 3d group, as compared to the 2d. Evidently, intake of PA led to complicated changes in fluid-electrolyte metabolism (including changes on the cellular level) related to an increase in flow of fluid and Na from the cellular space into tissues. The results of estimates and levels of this ion in extracellular fluid are indicative of the

possibility of accumulation of Na in tissues; in subjects with a positive balance it was at least 120 meq lower than the baseline (calculations made on the assumption of equal concentrations of Na in plasma and interstitial fluid; Na concentration in plasma was determined by G. S. Arzamasov). The results of our studies did not enable us to determine the exact tissues in which Na and fluid could accumulate, and to what extent their accumulation is reversible. The most probable site of deposition is connective tissue, the intercellular substance of which has the capacity for reversible binding of fluid and Na [7]. The histiocyte system of connective tissue may play some part in deposition of fluid [3]. A comprehensive study of redistribution of fluid and electrolytes in the body is considered to be an exceptionally important task, both for demonstration of mechanisms of adaptation to long-term HDT and to assess the efficacy of pharmacological correction of fluid-electrolyte metabolism. Since the volume of intracellular fluid and Na balance were elevated in 1 of the subjects of the 4th group, it can be assumed that Na and fluid retention during HDT is attributable not only to preventive agents, but individual distinctions of the subjects, most likely related to capacity of tissue for fluid and electrolytes. While deposition of fluid removed from the circulatory system occurs in the interstice [8] at the early stages of HDT, the demonstrated correlation between changes in Na balance and ICFV warrants the assumption that, with long-term exposure to HDT, there may be a change in fluid-electrolyte exchange between the interstice and tissues. This is indicated by the more marked decline in volume of extracellular fluid in the 1st group of subjects, as compared to the others, and ICFV in that group was increased already in all subjects on the 60th day of HDT. It can be assumed that part of the fluid that moved into the intracellular space in subjects of the 1st group originates from the interstice.

Table 1. Na balance as a function of changes in volumes of total body fluid, extracellular and intracellular fluid (M±m)

	Na, meq/ 120 days	ΔTFV, ℓ	ΔECFV, ℓ	ΔICFV, ℓ
I	−6,0±1,9	−3,5±0,5 (−6,7±1,0)	−2,5±0,4 (−13,0±1,5)	−1,0±0,4 (−3,1±1,7)
II	5,9±1,7	−1,3±0,2 (−2,8±0,6)	−2,1±0,6 (−14,6±1,9)	1,4±0,4 (5,2±1,1)
	$P<0,001$	$P<0,02$	—	$P<0,01$

Note: Percentile expression of parameters is given in parentheses. I and II—subjects with negative and positive Na balance, respectively.

Exercise had the opposite effect on Na balance and ICFV, as compared to pharmacological agents: both parameters were lower in the 2d group than in the 4th, and in the 3d group as compared to the 1st. The dissimilar effect of the preventive agents is apparently attributable to the fact that the "targets" for these factors are different. While cell metabolism is the target for PA, the main effect of exercise is related to maintaining the blood volume on a higher level, as indicated by the higher CPV in the 2d and 3d groups of subjects, as compared to the 4th and 1st, respectively. Such a difference in the preventive effects of the factors used offers a wide opportunity for combining them. The state of fluid-electrolyte metabolism by the end of the HDT period in the 3d

group should apparently be evaluated as the most favorable, since in this group the changes did not affect the intracellular space, while the decrease in plasma volume and losses can be compensated relatively easily by drinking water and taking salt, and redistribution of fluid in the interstitial space and blood stream.

Table 2. Changes in Na balance and fluid volumes as related to different preventive measures (M±m)

Subject group	ΔNa, meq/120 d	ΔTFV, %	ΔICFV,%	ΔECFV, %	ΔCPV, %	ΔIFV, %
1	4,9±1,8	−2,4±0,6	5,8±1,1	−15,0±2,4	−7,8±3,1	−16,7±3,[illegible]
2	−7,0±1,3	−8,5±1,3	−5,3±2,7	−13,8±3,2	3,0±9,6	−17,0±5,[illegible]
3	−5,7±2,7	−5,0±1,7	−0,6±3,0	−12,0±2,5	−3,4±3,5	−14,7±3,0
4	−3,7±8,4	−6,3±1,2	−1,5±2,7	−13,2±0,7	−4,0±2,7	−14,3±0,9
	$P_{2-1}<0,01$	$P_{4-1}<0,05$	$P_{4-1}<0,05$	—	—	—
	$P_{1-3}<0,02$	$P_{2-1}<0,01$				

The results of these studies warrant the conclusion that individual distinctions of fluid-electrolyte metabolism could be the cause of significant differences in reactions to long-term HDT. Quantitatively, these differences may be just as great as those elicited by the use of preventive agents. The high variability of all tested parameters in subjects using different preventive regimens indicates that intake of pharmacological agents that regulate mineral metabolism and exercise do not eliminate the individual distinctions referable to regulation of fluid-electrolyte status. Consequently, when elaborating individual preventive regimens, one must take into consideration individual distinctions related to the possibility of deposition of fluid and electrolytes in the different compartments for fluid in the body. In selecting and determining the dosage of preventive agents, one should strive toward minimizing their undesirable effects, which can be related to changes in volume, osmolarity or ion composition of the intracellular environment.

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BIOELECTRICAL ACTIVITY OF THE HEART AND BLOOD ELECTROLYTES IN ESSENTIALLY HEALTHY SUBJECTS SUBMITTED TO ANTIORTHOSTATIC HYPOKINESIA FOR 120 DAYS

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[Article by N. P. Artamonova, T. S. Zakharova, B. V. Morukov, G. S. Arzamazov and V. Yu. Semenov]

[English abstract from source] Electrocardiographic parameters and serum concentrations of potassium, sodium, calcium (total and ionized) and magnesium in 6 essentially healthy men, aged 30-45 years, were measured before, during and after 120-day head-down tilt at -4.5°. A close correlation was demonstrated between T-wave depression and serum concentrations of potassium (direct correlation) and calcium and magnesium (inverse correlation). No consistent changes in the sodium content during the 120-day test were seen. In spite of electrolyte changes in blood induced by head-down tilt, ECG variations showed minor hypokaliemia that was not followed by any clinical symptoms. These data can be used to evaluate the status of healthy people exposed to prolonged hypokinesia and to develop adequate prophylactic measures.

[Text] During long-term spaceflights there are changes in electrolyte metabolism [2, 18-19], which is one of the causes of changes in ECG parameters, and most often a decline of T-wave amplitude is observed [1, 4, 7, 8, 16, 20]. In some cases, American astronauts developed dysrhythmias which were tentatively attributed to hypokalemia [3, 4, 15].

Potassium ions play an important part in repolarization of myocyte membranes, influencing bioelectrical activity of the myocardium [5, 10]. Changes in heart function during long-term antiorthostatic [head-down tilt] hypokinesia (HDT) can be related to a significant extent to hypokalemia. This is indicated by the loss of potassium and nature of changes in the terminal part of the ventricular complex on the ECG (from decline to inversion of T wave) under hypokinetic conditions.

The correlation between changes in levels of potassium, sodium, calcium and magnesium in blood serum, as well as ECG parameters, has been studied in the presence of a number of internal diseases. At the same time, there has not been

sufficient investigation of the correlation between changes in cardiac activity and electrolyte metabolism with exposure to spaceflight factors [6, 17, 21].

Our objective here was to determine the correlation between change in blood serum electrolyte content and dynamics of electrocardiographic parameters in men submitted to long-term HDT.

Methods

These studies were conducted on 6 essentially healthy men 30 to 45 years of age, who were submitted to hypokinesia with head tilted down at an angle of -4.5° for 120 days. The ECG was recorded in the 12 conventional leads and the 3 leads of Nehb on a Mingograph-82 in the baseline period, on the 1st, 7th and 28th day of HDT, and every 2 weeks thereafter until termination of HDT, then on the 1st, 14th and 25th days of the recovery period. Blood was drawn from the ulnar vein 30 min after the ECG.

Potassium and sodium concentrations were measured by flame photometry, total calcium by titrometry, ionized calcium with ion-selective electrodes and magnesium, on a Saturn atom-absorption spectrophotometer.

Results and Discussion

Table 1 shows the dynamics of electrocardiographic parameters at different stages of 120-day HDT. The ECG changes were in the same direction in all subjects. On the 1st day of HDT, there was insignificant increase in heart rate (HR), after which it fluctuated within the range of baseline values. Starting on the 96th day, there was another insignificant increase in HR, which persisted to the 25th day of the recovery period.

There was no change in duration of atrioventricular and intraventricular conductivity during HDT. Duration of electric systole was essentially correlated with HR. We failed to demonstrate appreciable changes in amplitude of P waves, QRS complex and position of ST segment. At the same time, changes in T waves were noted in most leads. Starting with the 1st month of HDT, there was a tendency toward depression (particularly in the T_{II}, T_{V_2}, T_{V_5} leads), flattening and some widening (by 0.01-0.02 s) of T waves. The depression of T-wave amplitude became reliable on the 96th day.

During HDT, particularly in the second half of its duration, some subjects presented undulant changes in T waves, which appeared at different times. Transient deformity of T waves of the two-peak type in the central and left thoracic leads was observed in two subjects. O. G. Gazenko and A. D. Yegorov [3] had reported similar dynamics of T wave changes in cosmonauts during spaceflights, while B. M. Fedorov et al. did so with reference to ground-based studies with use of hypokinesia [12, 13].

On the whole, the ECG changes in all six subjects were typical of insignificant hypokalemia, which is not associated with clinical signs. As can be seen in Table 2, serum electrolyte content was in the normal range in all subjects before HDT. During hypokinesia, there was a tendency toward decrease in concentration of potassium and some increase in calcium (total and ionized) and magnesium. These electrolytes reached the baseline level by the 7th-25th day

Table 1. Dynamics of ECG parameters during 120-day HDT (M±m)

ECG param.	Baseline period	HDT, days									Recovery period, days	
		1	6	27	47	69	83	96	114	120	14	25
HR	56±4,59	69±4,77	56±3.53	57±4,23	67±1,94	58±3,53	60±3,17	70±3.00	61±5,47	62±7,55	60±2,51	77±7,07
QT	0,40±0,01	0,35±0,02	0,41±0,02	0,41±0.01	0,38±0,01	0,41±0,01	0,40±0,01	0,38±0,01	0,40±0,01	0,39±0,01	0,39±0,03	0,37±0,01
AT_{II}	0,40±0,07	0,37±0,06	0,31±0,08	0,34±0,06	0,29±0,04	0,30±0,06	0,25±0,05	0,27±0.05	0,24±0.04	0,21±0,09	0,36±0,12	0,40±0,06
AT_{aVF}	0,21±0,07	0,29±0.04	0,21±0,10	0,19±0,07	0,17±0,05	0,11±0,06	0,10±0,05	0,16±0.03	0,12±0,06	0,11±0,14	0,31±0,05	0,25±0,04
AT_{V_2}	0,85±0,13	0,66±0,11	0,72±0,12	0,73±0,10	0,61±0,09	0,59±0,08	0,57±0,12	0,48±0,06	0,49±0,04	0,50±0,12	0,60±0,12	0,56±0,19
AT_{V_5}	0,65±0,17	0,48±0,12	0,40±0,05	0,50±0,07	0,41±0,10	0,37±0,13	0,33±0,15	0,32±0,06	0,45±0,08	0,40±0,12	0,63±0,24	0,51±0,08

Table 2. Dynamics of blood serum electrolyte levels during 120-day HDT (M±m)

Electrolytes	Baseline period	HDT, days						Recovery period, days		
		27	47	69	96	114	120	7	14	25
Potassium, meq/ℓ	4,34±0,13	4,50±0,30	4,05±0,18	4,09±0,32	4,33±0,47	4,11±0,43	4,04±0,24	4,30±0,19	4,40±0,40	4,30±0,32
Sodium, meq/ℓ	142,6±1,9	148,6±2,7	145,3±3,8	145,9±4,2	141,0±1,6	144,4±1,4	143.8±2,5	140,9±2,9	—	139,7±1,6
Magnesium, meq/ℓ	1,69±0,10	1,69±0,06	1,78±0,08	1,77±0,10	1,88±0,09	1,78±0,11	1,79±0,09	1,72±0,09	1,70±0,08	1,70±0,07
Total calcium, meq/ℓ	4,73±0,07	4,93±0,07	4,90±0,06	4,95±0,06	5,03±0,07	4,98±0,09	4,88±0,05	4,76±0,07	4,73±0,08	4,66±0,05
Ionized calcium, mmol/ℓ	1,07±0,01	1,29±0,03	1,27±0,04	1,22±0,03	1,26±0,04	1,25±0,04	1,22±0,04	1,11±0,04	1,06±0,01	1,06±0,01

of the recovery period. There was no clearcut change in plasma calcium content. A correlation was demonstrated between ECG changes in T_{II}, T_{V2}, T_{V5} waves and changes in concentrations of electrolytes. The highest correlation with ECG parameters was demonstrable for magnesium (coefficient of correlation $r_{Mg\text{-}AT_{II}}$ = -0.90; $r_{Mg\text{-}AT_{V_{55}}}$ = -0.85; $r_{Mg\text{-}AT_{V_2}}$ = -0.80). For potassium and calcium, there was above-average correlation with ECG parameters ($r_{K\text{-}AT_{II}}$ = 0.75; $r_{K\text{-}AT_{V_2}}$ = 0.73; $r_{Ca\text{-}AT_{V5}}$ = 0.81; $r_{Ca\text{-}AT_{II}}$ = 0.72).

Analysis of individual ECG parameters and serum electrolyte content during and after 120-day HDT revealed that, in the vast majority or cases (94%), there was coincidence of dynamics of these parameters in all 6 subjects. It was learned that the decline in potassium content was associated with increase in calcium (total and ionized) and magnesium. The most appreciable depression of T-wave voltage coincided with the time of appearance of hypokalemia. At the same time, in one of the subjects, serum potassium concentration was above the baseline level on the 28th, 81st and 96th days of HDT, and in another subject serum potassium and magnesium on the 112th and 120th days of HDT were on the baseline level. In spite of this, the changes in T waves of these subjects presented the same distinctions as in the others. In our opinion, these exceptions cannot cause one to question the expounded view that ECG changes are a function of electrolyte content, since the level of serum electrolytes does not necessarily reflect intracellular and intratissular electrolyte content.

Thus, a comparison of changes in ECG parameters and blood electrolyte content in 6 essentially healthy men durihg 120-day HDT enabled us to find: 1) a decrease in potassium content and increase in calcium (total and ionized) and magnesium in blood serum; 2) a correlation between decline in serum potassium and depression of T waves on the ECG; 3) insignificant hypokalemia elicits only changes in T wave, but is not associated with clinical symptoms. The changes related to hypokalemia revert to normal rapidly in the recovery period.

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EFFECT OF IMMERSION HYPOKINESIA ON SOME PARAMETERS OF HUMAN MUSCLE POTENTIALS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 26 Aug 85) pp 27-31

[Article by L. G. Khristova, A. A. Gidikov, I. F. Aslanova, A. V. Kirenskaya, V. G. Kozlova and I. B. Kozlovskaya (People's Republic of Bulgaria and USSR)]

[English abstract from source] During 3-day immersion hypokinesia stimulation muscle potentials and averaged potentials of total EMG of m. biceps brachii were investigated in six test subjects. Stimulation potentials were obtained by exciting n. cutaneus with a train of square impulses. Potentials were recorded using a combined multi+electrode. Averaged potentials of total EMG were recorded by means of the same electrode. The propagation rate of the potentials, duration of their negative and end-positive phases as well as the length of their negative phase in space were measured. In addition, vector-electromyographic images of the potentials were recorded. After immersion hypokinesia the propagation rate decreased significantly, the duration of the end-positive phase increased and the length of the depolarized zone of potentials in space shortened. The decrease of the rate of propagation of stimulation potentials was 28% and that of averaged potentials of total EMG was 31% per group. These changes developed rapidly enough, indicating shifts in the properties of potentials of action of myofibers during immersion. Factors responsible for these changes are discussed.

[Text] The results of numerous studies conducted in actual weightlessness and model experiments served as the basis for development of conceptions of the important contribution of the zero gravity factor in the pathogenesis of motor disturbances observed under such conditions. The diminished influx of static stimuli, which play the leading role in the system of controlling tonic postural reactions [2], caused by this factor elicits a consistent decrease in tonus of antigravity muscles and, consequently, triggers a chain of reactions inherent in the atonic syndrome (diminished force of muscular contractions, dyscoordination, dysmetria, etc.).

It is known that changes in functional state of muscles are associated with consistent changes, in particular, in parameters of potentials of individual muscle fibers [6], potentials of individual motor units [4], evoked potentials [5] and averaged potentials on the overall electromyogram (EMG).

However, heretofore, the biophysical properties of muscles in weightlessness were beyond the field of vision of researchers, who concentrated mainly on the study of such functions as velocity and force properties and statomotor activity.

This is the first stage of implementation of a program of systematic investigations of biophysical properties of the muscular system in weightlessness.

We selected some parameters of evoked muscle potentials and averaged potentials on the overall EMG as characteristics to be studied. The potentials were recorded using special cutaneous electrodes. This method of recording is very simple, and it permits measurement of the most important parameters of muscle fiber activity under ordinary conditions.

The specific objectives of our work were: development of method of recording muscle potentials for use during water-immersion hypokinesia; investigation of parameters of muscle potentials reflecting the functional properties of muscle fibers, namely, rate of propagation of potentials over muscle fibers, duration of phases of muscle potentials, length of depolarization zone and its phases.

Methods

We used the model of "dry" immersion developed by Ye. B. Shulzhenko [3] as a factor simulating one of the main effects of weightlessness, removal of static load. The subject was placed in a tank, in horizontal position, on a sheet of fabric that separated him from the liquid. Water temperature was 33.4°C. Duration of exposure was 3 days.

The tests were conducted before and after immersion on 6 subjects; one of them was also examined on the 2d day of immersion. We studied the parameters of evoked potentials and averaged potentials on the overall EMG of the brachial biceps. During testing, the subject was supine on a cot, with his arm in extension and supination at the elbow.

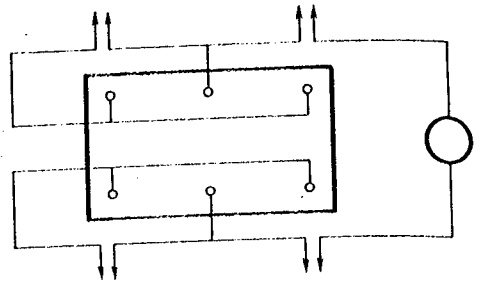

Figure 1.
Diagram of multi-electrode

To obtain evoked potentials, the cutaneous nerve was stimulated at a point between the heads of the brachial biceps with series of square-wave electric pulses (4 per series) lasting 0.1 ms at a frequence of 1 pulse/s. The intensity of stimulation was so chosen as to elicit distinct contractions of the brachial biceps. The potentials were derived using a previously described combined electrode. As can be seen in Figure 1, this electrode consists of 2 monopolar and 2 split electrodes 10 mm apart from one another. The area of the split and different poles of the monopolar electrodes did not exceed 1 mm^2. A round tin plate, 10 mm in diameter, served as the silent pole of the monopolar electrodes. The multi-electrode was attached over the distal part of the medial head of the brachial biceps at a distance of at least 20 mm from the motor zone of the muscle fiber ending. The active poles of the monopolar electrodes, which are also the central poles of the split electrodes,

are placed in parallel, while the poles of each of the split electrodes are perpendicular to the muscle fibers. The silent pole of the monopolar electrode is placed on the distal part of the forearm.

Potentials were amplified by a four-channel UBP 4-03 amplifier with frequency band of 0.01 to 10 kHz, and they were recorded on magnetic tape. The records were processed with Trakor and Medelek analyzers. During processing, we averaged four evoked potentials derived successively from the same electrode. The rate of propagation of evoked potentials (V_{st}) was measured by the duration of the interval (τ) between negative maxima of potentials (Figure 2) derived by means of 2 monopolar and 2 split electrodes. V_{st} of 10 mm/τ was calculated from the distance between electrodes, which was constant (10 mm). Duration (in ms) of negative and end positive phases was measured in potentials derived from the proximal split electrodes. The spatial length of negative phases of potentials was calculated by multiplying their duration by velocity.

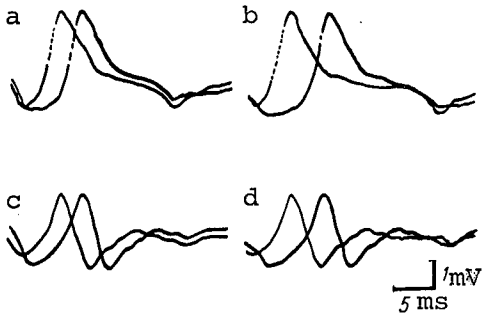

Figure 2.
Stimulation [evoked] and averaged potentials of overall EMG of brachial biceps before and after 3-day immersion
a, b) evoked potentials before and after immersion, respectively
c, d) averaged overall EMG potentials before and after immersion
a, b) monopolar lead
c, d) lead using split electrodes

Averaged potentials of the overall EMG were recorded using the same electrodes. Their characteristics were studied while subjects performed isometric contractions with 50% of maximum strength. We took 64 (or 128) segments of the overall EMG, which were averaged, for processing. On the EMG derived from the proximal split electrode, we arbitrarily selected a specific amplitude of negative potentials, achievement of which was a triggering signal for the EMG-averaging mode.

Averaging was done simultaneously in two channels derived from monopolar or split electrodes. For averaged potentials of overall EMG, we also determined the rate of propagation (V_{av}), duration of negative and end positive phases and spatial length of negative phase.

In addition, in both instances, we recorded the vectorelectromyographic image of potentials. For this purpose, two averaged potentials (evoked or obtained by averaging overall EMG) derived from either monopolar or two split electrodes were fed to horizontal and vertical amplifiers of the storage vectorscope.

Results and Discussion

With use of monopolar recording of evoked potentials, the stimulation artefact was rather large and distorted the tracing to some extent or other. In spite of this, the rate of propagation (V_{st}) measured in tests conducted with use of monopolar and split electrodes on the same subject differed by no more than 0.1 m/s. The same applied to rate of propagation of potentials of overall EMG (V_{av}). The difference between V_{st} and V_{av} of the same subject did not exceed 0.5 m/s, and in 4 out of 6 subjects, 0,2 m/s.

Mean duration and calculated length of negative phase of evoked and averaged EMG potentials before and after 3-day immersion

Leads	Before immersion		After immersion	
	time, ms	length, mm	time, ms	length, mm
	Stimulation potentials			
Monopolar electrodes	3,95±0,38	15,09±0,49	3,95±0,33	10,58±0,41
Split electrodes	3,74±0,31	14,29±0,43	3,62±0,37	9,77±0,46
	Averaged potentials			
Monopolar electrodes	3,85±0,41	15,36±0,48	3,87±0,29	10,68±0,35
Split electrodes	3,68±0,30	14,62±0,25	3,70±0,38	10,21±0,43

After 3-day immersion, all subjects presented a significant decline in rate of propagation of muscle potentials. While the rate of propagation of evoked potentials constituted 3.82±0.31 m/s before immersion, it was 2.70±0.31 m/s after. The decline, which constituted 28% for the group, was reliable ($P<0.02$). Mean velocity of propagation of averaged potentials of the overall EMG, which constituted 3.99±0.24 m/s before immersion, declined to 2.76±0.20 m/s after immersion. In this case, the decline constituted 31% and was also reliable ($P<0.01$, see Figure 2). As indicated by the data in the table, duration of the negative phase of stimulation and averaged muscle potentials did not change after immersion. However, due to the diminished rate of conduction, the length of the negative phase of potentials in space decreased with statistical reliability ($P<0.05$; see Table). Duration of the end positive phase of both evoked and averaged potentials of the overall EMG increased appreciably under the effect of immersion. It constituted 4.90±0.23 ms before immersion for stimulation potentials and 10.43±0.62 ms after. Duration of end positive phase of averaged potentials of overall EMG almost doubled.

Figure 3.
Vectorelectromyographic (VEMG) images of evoked and averaged potentials of overall EMG
a, b) VEMG images of stimulation potentials before and after immersion, respectively
c, d) VEMG images of averaged potentials of overall EMG before and after immersion

Analysis of vectorelectromyographic images of evoked potentials and averaged potentials of overall EMG also revealed changes in spatial characteristics of potentials. The results of these studies indicated that the potentials had sharper angles (Figure 3) in the vectormyographic images after 3-day immersion, which is indicative of diminished length of the depolarized zone of potentials.

Thus, the results of this investigation revealed that, during immersion, there are significant decline in rate of conduction of potentials, increased duration of end positive phase of stimulation potentials and averaged potentials of overall EMG, and diminished length of depolarization zone of potentials in space. These changes, which developed rather rapidly, are indicative of changes during immersion in properties of action potentials of muscle fibers. In particular, the increase in duration of the end positive phase could be due to increase in

in duration of action potentials. It could also be assumed that the increase in duration of end positive phase is caused by changes in synaptic transmission which desynchronized excitation of muscle fibers. However, the absence of change in duration of the negative phase of potentials indicates that this factor is not relevant. The stability of duration of negative phase, in spite of extension of the terminal positive phase, can also be readily attributed to the decline in rate of propagation of excitation over muscle fibers, which was demonstrated in this study. The diminished velocity is apparently also the cause of reduced length of the depolarized zone. The reduction in length of negative phase of muscle potentials and changes in form of vectorelectromyographic images are indicative of this assumption.

The causes of the demonstrated phenomena are not clear. Changes in fluid-electrolyte metabolism could be one of the possible factors involved in their development. However, the results of parallel studies revealed that sodium and potassium content of plasma did not exceed, during immersion, the range of their fluctuations in the baseline period.

It is a known fact that the rate of conduction of excitation is a function of muscle temperature. Indeed, a drop of body temperature was noted during immersion, but the magnitude of this decline [1] could not cause such a significant change in velocity. It can be assumed that impairment of trophic factors, which occurs as a result of diminished afferent influx in the absence of a static load, with atonia and virtually no motor activity, plays a leading role in development of the demonstrated changes.

Further investigations are needed to clarify the mechanisms of development of changes in skeletal muscles.

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CHANGE IN BILE ACID AND LIPID CONTENT OF HUMAN BILE DURING EXPOSURE TO ANTIORTHOSTATIC HYPOKINESIA AND ITS CORRECTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 31 Jul 85) pp 31-37

[Article by I. L. Medkova, O. V. Zhiznevskaya, K. V. Smirnov, V. I. Lebedev and Ye. M. Artamasova]

[English abstract from source] The spectrum of bile acids and bile lipids in men exposed to 120-day head-down tilt was investigated. The test subjects were subdivided into four groups: group 1--bed rest per se, group 2--bed rest + exercise, group 3--bed rest + drugs normalizing calcium metabolism, and group 4--bed rest + exercise + drugs. It was anticipated that biliary concrements would primarily be formed in group 1 and 2 subjects. They showed a low level of bile acids and a high content of total Ca and cholesterol in the bile, which was more pronounced in the C portion (decrease of the cholate/cholesterol coefficient). Group 2 subjects displayed a modified synthetic function of the liver: prevalence of tauroconjugates in the bile (decrease of the ratio of glucoconjugates to tauroconjugates). Group 3 and 4 subjects showed a faster synthesis of bile acids in the liver and a lower content of total calcium and cholesterol in the bile, the latter being more distinct in group 4 subjects. Positive dynamics of these parameters is a factor responsible for a reduced lithogeny of the bile. However, the test subjects of these groups exhibited hazardous changes that may be responsible for concrement formation. This is indicated by a lower concentration of the lipid complex in the bile, possibly at the expense of a lower content of phospholipids. This emphasizes the necessity of further search for prophylactic procedures aimed at normalizing the synthetic function of the liver under hypokinetic conditions.

[Text] The results of studies conducted previously revealed that there are specific changes in processes of hydrolysis, absorption and transport of lipids under hypokinetic (HK) conditions. This is apparently attributable to a change in activity of lipolytic enzymes, which hydrolyze fats, and bile-synthesizing function of the liver [4, 7, 8]. There is decrease in bile lipid complex secretion by hepatocytes, there is change in amount and nature of conjugation of bile acids which, combined with the decrease in lipid complex concentration,

could lead to changes in colloid stability of bile [2, 4]. The hypercholesterolemia observed with limited motor activity also causes changes in biosynthesis of bile acids, since one of the means of removing excessive cholesterol from the body is to convert it into bile acids.

It has been demonstrated that interaction between bile acids and Ca^{2+} ions in bile causes them to bind, which prevents formation of insoluble calcium deposits. The changes in Ca metabolism associated with HK (hypercalcemia, development of negative calcium balance, depression of bone demineralization [1, 5]), combined with changes in biosynthesis of bile acids can, in turn, lead to increased lithogenicity of bile.

These facts served as grounds for a special investigation of bile-synthesizing function of the liver and bile calcium content during long-term antiorthostatic HK with use of various means of correcting Ca metabolism under these conditions.

Methods

The investigations were conducted on 15 essentially healthy men 30 to 40 years of age who were kept on strict bedrest in antiorthostatic [head-down tilt] position (tilt angle of -4.5°) for 120 days. The subjects were divided into four groups: the 1st (control) consisted of 3 men who remained under HK conditions without use of preventive measures; the 2d, 4 people who performed a set of physical exercises during HK; 3d, 4 men who received a set of pharmacological agents, among which xidiphone was used to normalize Ca metabolism and systems of its regulation on a program that was developed and proposed by A. I. Grigoryev and B. V. Morukov; the 4th group consisted of 4 people who performed exercises in addition to intake of xydiphone.

The duodenum was probed in the baseline period, then on the 20th, 67th, 90th and 112th days of HK and on the 7th and 20th days of the recovery period (RP). Quantitative assays of bile acids and bile lipids were performed in the B and C portions by thin-layer chromatography on Silufol sheets [3], followed by densitometry in reflected light. The lipid complex was identified by the method of M. F. Nesterin et al. [6]. The bile sample (liquid phase with sediment) was ashed before assaying total Ca. Calcium was measured by atom-absorption spectrometry on a Perkin-Elmer 306 spectrometer.

Results and Discussion

On the 20th day of hypokinesia, the 1st group of subjects presented an increase in taurocholic acid (TCA) content in both portions of duodenal contents (see Table). By the end of the HK period, the concentration of this acid in B and C portions of bile was close to baseline values, whereas in the RO it was below the baseline level. Taurodeoxycholic + taurochenodeoxycholic acids (TDCA + TCDCA) showed elevation in both portions of bile in subjects of the 1st group at the start of HK with subsequent decline to below the baseline level by the 90th-112th day of HK and in the RP. In the same group, a significant increase was noted in glycocholic acid (GCA) content in both portions of duodenal contents on the 20th day, and the changes were highly reliable in portion B ($P<0.001$). By the end of HK and in the RP, there was reliable decline of GCA level in the B portion. In the C portion of bile, there was also a tendency

Changes in bile acid content of human bile during hypokinesia with head-down tilt and their correction

Acid	Baseline		Bedrest day 20		67		90	
	B	C	B	C	B	C	B	C
				First group				
TCA	245,6±20,1	136,4±19,7	364,4±64,5	443,8±203,8	352,2±100.7	87.9±30.7	304,8±60.3	—
TDC+TCDC	391,6±95,7	264,9±86,9	738,3±52,8*	404,2±102,8	423,3±97.9	151.3±34.0	282,4±110.1	—
GCA	762,9±37,1	382,4±110,2	2097,8±124,9*	990,3±262,3	750,4±206.5	832,1±262.9	423,7±49,7*	—
GDC+GCDC	668,0±94,8	344,0±62,2	1016,0±398,4	898,0±253,0	501.8±144.4	425,4±160.5	245,6±21,5*	—
				Second group				
TCA	298,3±94,6	164,0±5,1	284,0±90,4	606,1±90,1*	966,4±247,2	274,4±32,9*	518,0±155,9	387,8±48,7*
TDC+TCDC	350,7±80,9	225,7±14,1	644,2±164,2	581,1±54,1*	421,1±150.9	445,5±67.6*	548,8±89,3	319,3±7,0*
GCA	961,8±197,4	567,0±213,0	1295,8±100,2	1422,9±28,1*	901,0±343.4	1278,3±42.7*	1087,1±370,1	313,5±9,2
GDC+GCDC	707,5±151,9	483,7±45,9	759,6±94,8	874,5±143,5	482,7±63.7	616,7±181,2	783,9±124.9	227,9±51,7*

Bedrest day 112		Recovery period day 7		20	
B	C	B	C	B	C
238,9±59,0	149,2±19,4	139,7±41,5	162,2±39,1	153,5±43.7	70,6±14,5
287,2±76,8	153,2±43,4	143,8±34,7	220,4±80,1	112,7±20,1	90,2±24,0
444,4±106,95*	320,7±114,5	320,0±90,3*	666,9±291,0*	167,9±0.4*	542,8±198,8
228,8±66,2*	294,1±86,2	169,7±36,3*	—	263,9±30.7*	380,9±119,4
677,5±138,7	179,5±82,3	534,8±252,8	129,3±48,3	62,8±14,9	—
610,9±180,0	201,2±52,8	555,3±133,4	201,3±52,8	108,2±33.6	—
1316,1±262,8	703,5±39,9	1200,3±190,1	483,1±50,8	476,8±40.3	—
548,7±45,9	570,4±64,8	810,6±183,7	500,1±119,4	427,8±77,7	—

Table (continued)

Acid	Baseline		Bedrest day					
			20		67		90	
	B	C	B	C	B	C	B	C
				Third group				
TCA	188,5±20,2	138,6±18,4	373,8±93,4	201,6±75,5	299,0±57,0	249,1±48,3	543,8±251,8	244,3±99,1
TDC+TCDC	318,7±63,5	198,1±31,1	514,8±103,0	204,2±57,3	473,7±73,3	291,1±75,7*	426,0±84,6	165,5±47,9
GCA	890,9±113,0	430,6±61,1	1555,7±464,1	264,4±112,2	1108,8±101,2	625,5±189,3	946,1±117,6	317,5±65,6
GDC+GCDC	502,1±62,6	122,6±24,2	1058,9±210,7*	61,2±9,1*	579,4±31,4	521,5±175,5	606,4±170,6	219,1±64,4
				Fourth group				
TCA	268,4±90,6	134,8±23,7	448,6±181,6	188,4±71,1	429,1±109,6	616,9±175,4	—	462,9±162,7
TDC+TCDC	366,6±95,0	128,3±24,4	601,6±355,4	174,2±55,8	485,0±90,1	501,4±171,6	—	277,7±97,5
GCA	927,4±200,9	420,3±120,9	467,3±106,3	470,8±110,7	1331,3±264,5	1454,0±320,7*	—	422,7±135,2
GDC+GCDC	910,0±250,0	331,7±23,5	853,5±202,0	103,7±17,8*	815,9±159,7	476,6±89,3	—	448,3±148,6

661,0±16,8*	558,3±141,0*	76,2±42,5	139,5±42,7	133,5±40,7	111,4±32,7
471,5±124,7	58,5±15,1*	166,9±40,0	121,8±39,2	133,4±41,4*	88,2±37,8
527,4±162,9	803,7±118,7*	621,3±194,1	354,7±103,4	601,6±166,8	336,5±95,9
272,4±116,5	437,5±63,7*	856,6±214,7	244,9±62,6	435,9±161,0	252,4±103,6
779,3±243,2	276,5±85,2	339,9±85,7	139,7±44,2	124,3±20,9	—
545,8±66,5	297,6±58,7*	338,1±113,8	127,2±38,7	134,8±54,4	—
1093,0±1,6	533,2±123,3	1055,6±331,8	483,1±184,9	689,2±184,0	—
682,9±223,3	382,9±73,8	765,0±22,2	422,2±152,2	360,8±130,0	—

*Differences are reliable in comparison to baseline.

toward decline of GCA on the 67th day of HK and approximation of its level to the baseline on the 112th day of the study. The 7th day of the RP was characterized by drastic and reliable ($P<0.001$) elevation of the level of this bile acid. In the 1st group of subjects, glycodihydroxycholanic acids (GDCA + GCDCA [glycochenodihydroxycholanic acid]) in the B portion increased significantly on the 20th day of HK, whereas starting on the 67th day of HK and in the RP it dropped below the baseline level, with a high degree of reliability. The dynamics of changes in GDCA+GCDCA in the C portion of bile were analogous in the C portion of bile to those of the B portion.

Total bile acids in both portions of duodenal contents presented an increase on the 20th day of HK in the 1st group of subjects, with subsequent gradual decrease at all tested times. On the 67th and 90th day, testing revealed a drastic decline of glycoconjugate to tauroconjugate ratio (GC/TC) in portion B due to increase in tauro acid content. Subsequently, this ratio changed insignificantly. Gradual increase of this coefficient was observed in the C portion of bile on the 20th and 67th days of HK, to 5.2 (versus 1.8 in the baseline period) due to increase in amount of glycoconjugates. By the end of the HK period, the GC/TC ratio reverted to normal, but on the 20th day of the RP it showed another drastic increase. In the same group, there was decline of cholate-cholesterol ratio during HK, attributable more to increase in cholesterol content in the C portion and to decrease in cholate content in the B portion. In addition, starting on the 67th day of HK, there was increase in ratio of phospholipids to cholesterol (PL/CS) in both portions of bile. Assays of lipid complex concentration revealed a decline in bile, which was reliable for the C portion on the 90th day of the study. The 1st group of subjects showed an increase in percentage of Ca in both portions of bile, particularly at the end of the study.

Investigation of the dynamics of changes in tauroconjugates in the 2d group of subjects revealed an increase in both portions of bile during the experiment, with subsequent decrease in the RP. GCA content increased in this group in both portions of bile, more drastically and reliably in the C portion. On the 67th day of HK, there was decline of GCA to below baseline values, with persistence of reliable increase in the C portion. Starting on the 90th day of HK and in the RP, there were phasic changes in GCA content of bile (see Table). GDCA+GCDCA showed little change in the B portion in the 2d group of subjects during HK. The C portion showed insignificant increase in concentration of these acids on the 20th experimental day with reliable decrease by the 90th day ($P<0.05$).

In the B portion of duodenal contents, total bile acids showed a rise in the experimental period with decline on the 20th day of the RP. In the C portion, there was drastic increase in total bile acids on the 20th day of HK, with gradual decrease to baseline values at subsequent tested times. In the same group of subjects, gradual decline of GC/TC ratio was demonstrated by the 67th day, with GC going to 1.0 (versus 2.6 in the baseline period). This ratio increased on the 90th and 112th days of HK, as well as on the 7th day of the RP, but was still below baseline values. The 20th day of the RP was characterized by drastic increase in GC/TC ratio.

Insignificant changes were demonstrated in conjugate ratio at the start of HK in the C portion. On the 90th day, there was drastic decline of GC/TC, and

by the 112th day it showed normalization. In the B portion of the 2d group of subjects, some increase in the cholate-cholesterol ratio was found by the end of the HK period and dramatic decline of this parameter in the RP; the C portion presented insignificant elevation of its level on the 20th day of HK, with gradual decline by the 67th and 90th days of HK due to decrease in cholate content and increase in cholesterol. In addition, this group of subjects presented significant decline of PL/CS ratio. There was a tendency toward decrease in lipid complex content of the bile at different stages of the study. The 2d group of subjects presented undulant changes in percentage of Ca in both portions of bile: periods of dramatic increase (on the 67th and 112th days of HK) alternated with a drop in Ca percentile content (on the 90th day of HK and in the RP).

The subjects in the 3d group presented gradual elevation of tauroconjugate level in both portions of bile, followed by a decline toward the end of the study and in the RP of the C portion. This group of subjects also presented a tendency toward increase in glycoconjugate content of bile. Reliable changes were demonstrated in the C portion on the 112th day of HK.

In general, overall bile acid content in subjects of the 3d group presented a tendency toward increase in both portions of bile, and it was more marked by the end of HK. GC/TC ratio dropped the most significantly in this group of subjects on the 90th day of the study in the B portion (to 0.7, versus 2.8 baseline). In the C portion of duodenal contents in the 3d group of subjects, GC/TC changed similarly to the findings in the 2d group. Examination of cholate-cholesterol coefficient revealed a rise toward the end of the HK period in B and C portions of bile. In both portions, there was a tendency toward increase of PL/CS ratio during HK and the RP. The same group of subjects showed a decrease in concentration of lipid complex in the B portion during HK and in the RP, as well as decline of Ca percentage to 30.4% of the baseline on the 90th and 112th days of HK. Conversely, on the 67th day the C portion showed dramatic (to 420%) increase in total Ca content, followed by a decline toward the end of the HK period to 71%. In the RP, the percentage of Ca in this bile portion was double the baseline value.

The 4th group of subjects presented an increase in tauroconjugate content in both portions of bile under HK conditions. Examination of glycoconjugates revealed that the concentration of GCA in the B portion of duodenal contents dropped to one-half on the 20th day of the study. No appreciable changes were demonstrable in the C portion. On the 67th day of HK, there was a quantitative jump in GCA content of both portions of bile, and it was reliable in the C portion. On the 90th and 112th days of the study and on the 7th day of the RP, there was a tendency toward decline in level of this acid in portion B and normalization in portion C. There was insignificant change in parameter of glycodihydroxycholanic acid levels in the B portion during HK. In the C portion, there was a reliable decline of levels of these acids ($P<0.02$) in the C portion on the 20th day of HK, followed by elevation toward the end of the HK period.

Insignificant increase in total bile acid content toward the end of HK and its subsequent noramlization in the RP was demonstrated in both portions of bile in the 4th group of subjects. In the B and C portions in this group, the GS/TC ratio changed in an undulant fashion throughout the test period. In addtion, there was increase in the cholate-cholesterol coefficient due to increase in

cholate content. In this group, there was an increase in PL/CS ratio at different stages of HK, particularly in portion C, due to decline of cholesterol level. There was a decrease in concentration of lipid component in both portions of bile throughout the HK and RP periods. Changes in percentile content of Ca in the bile were similar to the dynamics of this parameter in the 3d group of subjects; however, the rise in Ca content of the bile was less significant in them.

Thus, the results of these investigations revealed that overall bile acid content diminishes toward the end of the bedrest period in the 1st group of subjects, and in those of the other groups there is elevation of the parameter of total glycoconjugates and tauroconjugates in bile.

Assays of serum cholesterol ester levels in the same study on subjects of the 1st group revealed dramatic and reliable elevation starting on the 72d day of the study. This, along with the decrease in bile cholates, is indicative of impaired transformation of cholesterol into bile acids under HK conditions.

In the 2d-4th groups, with use of preventive measures (pharmacological agents and exercise), hypercholesterolemia was not demonstrated, and this could be related to optimization of the process of bile acid synthesis from cholesterol.

We could expect the greatest probability of development of concretions in bile in the 1st and 2d groups of subjects. The low level of bile acids was associated with high levels of total Ca and cholesterol in bile, more so in the C portion (decline of cholate-cholesterol ratio). Prevalence of tauroconjugates in bile (decline of GC/TC) was a manifestation of change in synthetic function of the liver in the 2d group of subjects.

In the 3d and 4th groups, there was increased synthesis of bile acids, decreased total calcium and cholesterol content of the bile, more marked in the 4th group. The positive dynamics of these parameters is a factor in decline of lithogenicity of bile; however, even in these groups we observed a number of changes presenting a danger with respect to concretion formation. This is indicated by the decrease in concentration of lipid complex in bile, perhaps due to decrease in phospholipid content. This indicates that it is necessary to pursue further studies in order to find preventive measures for normalization of synthetic function of the liver under hypokinetic conditions.

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QUANTITATIVE STUDY OF OSTEOBLASTS AND OSTEOCLASTS OF RAT BONES WITH SIMULATION OF WEIGHTLESSNESS

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[Article by G. N. Durnova, Z. F. Sakharova, A. S. Kaplanskiy, V. M. Ivanov and M. S. Khaydakov]

[English abstract from source] Tibia and vertebrae of rats exposed to hypokinesia or head-down suspension were investigated by quantitative histomorphometry. It was found that 35- and 60-day hypokinesia as well as 35-day suspension caused osteoporosis in the tibial and vertebral spongiosa. The development of osteoporosis was accompanied by a significant reduction in the number of osteoblasts in the primary spongiosa of tibia and vertebrae whereas no noticeable changes in osteoclasts were observed either in hypokinetic or suspended rats. The only exception was lumbar vertebrae in which the amount of osteoclasts decreased as a result of 60-day hypokinesia. It is assumed that the reduction in the number and activity of osteoblasts plays the major part in the development of osteoporosis during hypokinesia and suspension.

[Text] Experiments aboard biological earth satellites of the Cosmos series indicate that a decrease in functional load on the skeletomuscular system in weightlessness elicits impairment of the normal process of bone formation and leads to development of osteoporosis [2, 5, 8-11, 13]. Since formation de novo of bone tissue and its resorption depend appreciably on the number and functional activity of osteoblasts and osteoclasts, it can be assumed that changes in these cell populations play a significant role in development of osteoporosis. We submit here the results of histomorphometric studies of the tibia and lumbar vertebrae of rats, in which a reduction of loads on the locomotor system was induced in ground-based model experiments simulating weightlessnes, special attention being given to the quantitative ratio between osteoblasts and osteoclasts.

Methods

Experiments were performed on 60 male Wistar rats weighing 240-270 g. The functional load on the skeletomuscular system was reduced by placing the animals for 35 and 60 days in tight box-cages or suspending them by the tail

to a movable unit in such a way that the hind limbs would not touch the bottom of the cage and would carry no load at all. The forelegs served for support in part, and the rats could use them to move around the cage. This method of "suspending" rats in antiorthostatic position, which was proposed by Ye. A. Ilyin and V. N. Novikov [3], permits removal of static and dynamic loads from the posterior extremities, as well as to elicit the redistribution of blood in the body that is inherent in weightlessness. Control rats were kept under vivarium conditions. After the experiments, the rats were weighed and sacrificed using a guillotine. Muscle tissue was removed from the tibia and lumbar vertebrae, calipers were used to measure the length of the tibia, and the bones were fixed (2 days) in 4% neutral formalin prepared in 10% EDTA, the pH of which was brought up to 7.0 with 1 n NaOH. The bones were decalcified in 10% EDTA, pH 7.0, after which they were washed thoroughly in water, dehydrated in alcohol and imbedded in histoplast. Serial sections of the bones, 5-7 μm thick, which were cut parallel to the long axis at 25-50-μm intervals, were stained with hematoxylin and eosin, picrofuchsin after van Gieson and methyl green-pyronine after Brachet. The osteoblasts and osteoclasts were counted in 15-20 microscope fields just under the epiphysial cartilage growth plate at 630× magnification, using for this purpose preparations stained with methyl green-pyronine. When counting osteoblasts, we considered only functionally active cells, i.e., polygonal and spindle-shaped cells with extensive pyroninophilic cytoplasm and eccentric nucleus. In the osteoclast population, we counted not only giant multinuclear cells, but those with one or two nuclei and pale pink foamy cytoplasm. We also made histomorphometric evaluation of the volume density of primary and secondary spongiosa, width of the epiphysial cartilaginous growth plate and width of the primary spongiosa zone. Relative density of primary and secondary spongiosa was determined by the point method using the morphometric grid of S. B. Stefanov, while the width of the epiphysial cartilaginous growth plate and zone of primary spongiosa was determined using an MOV-15 ocular microscope in 10 areas in the middle of the section of tibia or vertebra. The obtained digital data were submitted to statistical processing according to Student. All digital data were expressed as percentages of the appropriate vivarium control.

Results and Discussion

Quantitative histomorphometric analysis of normal tibia and lumbar vertebrae revealed that the width of growth plate and zone of vertebral primary spongiosa is narrower, while volume density of primary and secondary spongiosa is higher than in the tibia. The number of osteoblasts is considerably lower in the zone of primary vertebral spongiosa than in tibial bones, whereas the number of osteoclasts is about the same.

Histomorphometry of the tibia and vertebrae of rats revealed that 35- and 60-day clinostatic hypokinesia or suspension leads to development of osteoporosis. This is indicated by the significant decrease in volume density of primary and secondary spongiosa (see Table). With clinostatic hypokinesia, reduction of spongiosa in the tibia increased with increase in duration of the experiment. In addition to reduction of volume density of primary and secondary spongiosa, the experimental groups of animals presented some decrease in length of the tibia, as well as narrowing of the epiphysial cartilaginous growth plate and zone of primary spongiosa in both the tibia and vertebrae (see Table). Narrowing of the epiphysial cartilaginous growth plate occurred due to decrease in

height of cartilage cell columns and thickness of zone of swelling and decalcification of cartilage, while the decrease in volume density of primary and secondary spongiosia is due to decrease in number, length and width of osseous trabeculae.

Results of histomorphometric studies (%) of tibia and lumbar vertebrae of rats submitted to clinostatic hypokinesia and suspension

Parameter	Hypokinesia			Suspension	
	35 d	60 d			
	tibia	tibia	vertebra	tibia	vertebr.
Bone length	—	—4	—	—3	—
Width of growth plate	—25*	—17*	—14*	—8	—12*
Width of primary spongiosa zone	—51*	—42*	—69*	—34*	—22
Spongiosa volume density:					
primary	—21*	—53*	—38*	—8*	—14*
secondary	—55*	—56*	—22*	—40*	—30*
Osteoblasts	—42*	—49*	—36*	—22*	—35*
Osteoclasts	+22	+21	—36*	+18	+12

*Statistically reliable differences between control and experiment.

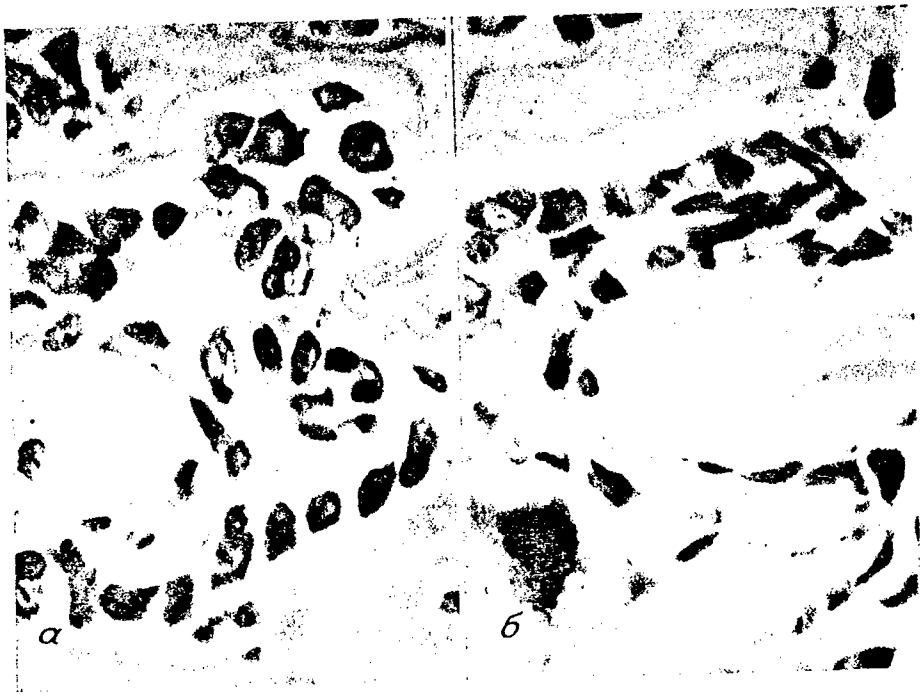

Figure 1. Osteoblasts in rat tibia primary spongiosa; hematoxylin and eosin stain; lens 60×, eyepiece 6.3× magnification

a) active osteoblasts with profuse cytoplasm covering the surface of trabeculae under normal conditions
b) decreased number of osteoblasts with prevalence of inactive spindle-shaped cells

Determination of number of osteoblasts revealed that with both clinostatic hypokinesia and suspension there is a statistically reliable decrease in number of osteoblasts in the primary spongiosa zone, in both the tibia and vertebrae. While there is normally prevalence of polygonal cells among osteoblasts, with profuse and RNP [ribonucleoprotein]-rich cytoplasm that is strongly stained by pyronine (active osteoblasts), in the case of hypokinesia and suspension, along with active osteoblasts, fusiform cells with moderately pyroninophilic cytoplasm (intermediate forms) and flat cells with mildly pyroninophilic cytoplasm were encountered considerably more often (Figure 1). The latter are cells with low activity, according to the classification of C. G. Woods [15]. There was also some change in localization of osteoblasts, small groups of which were demonstrable in the spaces between primary spongiosa trabeculae. Normally, the osteoblasts are arranged in the form of one row of cells on the surface of bone trabeculae.

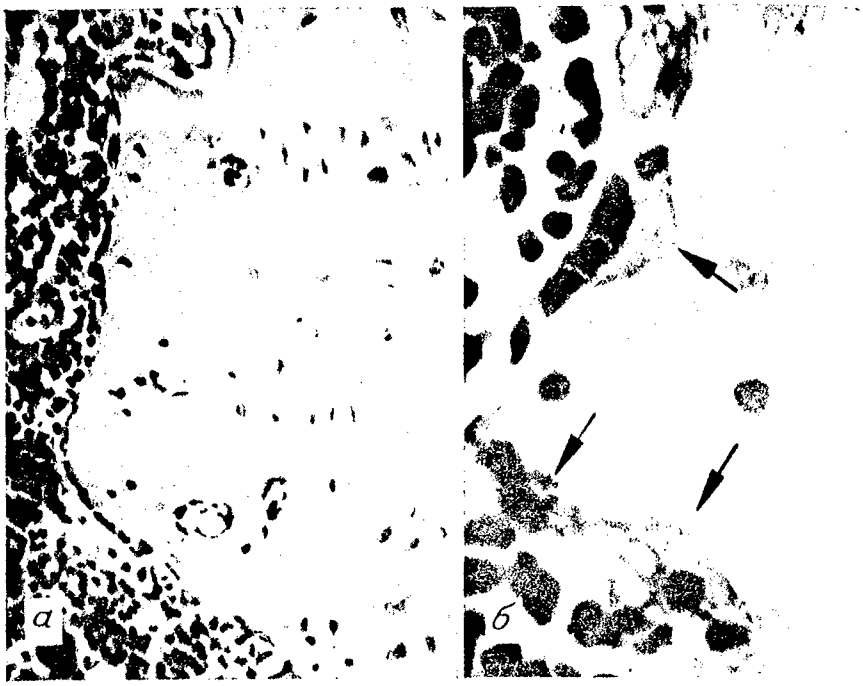

Figure 2. Activation of primary spongiosa resorption in rat tibia with 60-day clinostatic hypokinesia

a) appearance of "clipped" trabeculae in primary spongiosa zone; hematoxylin and eosin stain; lens 20×, eyepiece 6.3×
b) osteoclasts on surface of clipped trabeculae resorbing bone tissue; hematoxylin and eosin stain; lens 60×, eyepiece 6.3×

Unlike osteoblasts, no statistically reliable changes were demonstrable in number of osteoclasts in the tibia of rats submitted to hypokinesia or suspension. There was a decrease in number of osteoclasts in the lumbar vertebrae after 60-day hypokinesia. Morphologically, the osteoclasts in the spongiosa of experimental groups of rats did not differ from those of control animals. It should be noted that trabeculae of primary spongiosa that appeared to have clipped apices, the surface of which was lined with osteoclasts (Figure 2), were consistently

observed in the tibia of rats submitted to long-term hypokinesia. In the opinion of some authors [9], such histology of primary spongiosa is indicative of intensification of the process of bone resorption; it was observed in rats submitted to weightlessness aboard biosatellites.

Analysis of the results of morphometric studies of tibial and lumbar vertebral spongiosa of rats submitted to hypokinesia and suspension led us to the conclusion that, in both instances, there is development of osteoporosis, which is very consistent with the results obtained by other authors, who reported development of osteoporosis when animals' movements were restricted 1, 2, 4] or their limbs were deprived of static loads [2, 5-11, 9, 13-14].

Development of osteoporosis in the spongiosa of the tibia and lumbar vertebrae during hypokinesia and suspension is, according to our data, due primarily to inhibition of bone growth and neosynthesis. This is indicated by the reduction in length of the tibia, width of epiphysial cartilaginous growth plate and height of chondrocyte columns, width and volume density of primary spongiosa, as well as significant decrease in number of functionally active osteoblasts in the region of primary spongiosa. The question of whether there is also a change in level of bone resorption, along with inhibition of neosynthesis of bone, during hypokinesia or suspension of rats remains unclear, since no statistically reliable changes were demonstrable in number of osteoclasts (with the exception of a decrease in their number in vertebrae of hypokinetic rats). It is also difficult to answer this question because the number of osteoclasts, according to available data, does not necessarily show a correlation to their functional activity, as a result of which there may be inhibition of the resorption process in the presence of increase in number of osteoclasts [12]. Unlike the data we obtained, which indicated that there was no appreciable change in number of tibial osteoclasts with 35-day suspension of rats, the results of other studies [14] pertaining to a similar experiment lasting 14 days indicated a 90% increase in number of osteoclasts in the tibial spongiosa. The cited studies related this phenomenon to elevation of glucocorticoid level in blood due to development of an acute stressor reaction. Evidently, we should seek the cause of the above-mentioned discrepancy of findings in the difference in duration of experiments (since the acute phase of the stress reaction observed on the 14th experimental day could have disappeared by the 35th day), as well as the more stressogenic effect of the suspension model used by Morey.

If we compare the results of histomorphometric studies of the rat tibia and vertebrae during hypokinesia and suspension, we can conclude that osteoporosis develops in both instances. With hypokinesia, more severe changes develop in the spongiosa than after suspension of the same duration, in spite of the fact that, with suspension, the load is removed from the posterior extremities to a considerably greater extent than with hypokinesia. This finding, which seems a contradiction at first glance, can apparently be attributed to the fact that the stress reaction, the severity of which is greater with hypokinesia than suspension, as indicated by the decrease in weight of the body, thymus and splee makes some contribution to development of osteoporosis with hypokinesia and suspension.

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HYDROLYSIS, TRANSPORT AND UTILIZATION OF CARBOHYDRATES IN RATS WITH RESTRICTED MOTOR ACTIVITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 29 Apr 85) pp 41-47

[Article by L. G. Goland-Ruvinova, R. A. Pechenkina, N. P. Goncharova, and K. V. Smirnov]

[English abstract from source] Carbohydrate hydrolysis, transport and utilization were investigated in rats exposed to diminished motor activity for 90 days. Glycemic curves were examined using provocative tests with equivalent quantities (1.5 g/kg body weight) of poly-, oligo- and monosaccharides (starch, maltose, glucose). Simultaneously, carbohydrases were measured in the homogenates of the pancreas, duodenal mucosa and small intestine as well as radioimmune insulin and glucagon were determined in blood. In the course of hypokinesia carbohydrate hydrolysis, transport and utilization varied in a different manner. At the beginning of exposure the activity of carbohydrases responsible for carbohydrate hydrolysis in the cavity and membranes increased which was accompanied by hyperglycemia and rapid utilization of carbohydrates. This is associated with nonspecific reactions to hypokinesia and higher requirements of the body for the energy substrate. By hypokinesia day 30 carbohydrate hydrolysis and transport were inhibited, hypoglycemia developed but glucose utilization remained unchanged. At a later stage of exposure the system of carbohydrate hydrolysis and transport showed an adaptive reaction; inhibition of pancreatic amylase was accompanied by accelerated enzyme transport in the small intestine and glucose resorption. In this situation the glycemic curves became extended suggesting a delay in glucose utilization. The latter was induced by changes in the endocrine compartment of the pancreas.

[Text] Long-term absence of adequate load on the muscular system leads to a decline in carbohydrate metabolism of the glycolytic and, particularly, oxidative type. Blocking of glycolysis and tricarboxylic acid cycle causes a compensatory increase in oxidation of carbohydrates in the pentose cycle. There is more intensive involvement in energy metabolism of the concrete energetic substrate--fatty acids [3]--to replace the macroerg deficiency. For this reason, glucose homeostasis changes [6].

There are a few studies [7] dealing with the nature of glycemic curves, which are the integrative indicator of glycemia, when motor activity is limited. The glycemic curve reflects the state of the body's physiological systems responsible for homeostasis of glucose in the body, including the functional state of the exocrine and endocrine systems of the digestive tract. In this regard, it is desirable to make a combined study of glycemic curves following carbohydrate loads, activity of enzymes that effect the different stages of hydrolysis of carbohydrates, levels of insulin and glucagon in blood.

We submit here the results of a comprehensive study of the systems of hydrolysis, transport and utilization of carbohydrates in rats in the course of long-term exposure to the factor of restricted motor activity.

Methods

These studies involved acute and chronic experiments on male white rats weighing 160-180 g whose movements were restricted for 90 days. The animals were placed in special plexiglas box-cages that limited their motor activity. The rats were given feed in pellet form and water ad lib.

To study the glycemic curves, we used functional tests with equivalent amounts (1.5 g/kg body weight) of polysaccharides, oligosaccharides and monosaccharides (starch, maltose, glucose) used as loads. The functional load tests with different carbohydrates permit examination of cavitary and membrane hydrolysis of carbohydrates, transport of glucose obtained by hydrolysis of starch and maltose, resorption function of the small intestine and utilization of glucose by body tissues. The glycemic curve with a polymer--starch--load characterizes the functional state of the exocrine part of the pancreas, sorption properties of the surface of the small intestine and state of the enzyme systems of the maltase group. The glycemic curve with a maltose curve is an indicator of activity of enzyme-transport encembles of epitheliocytes, which effect coordinated hydrolysis of dimers and nutrient transport. The glycemic curve with a glucose load permits evaluation of the functional state of the system of resorption.

Blood glucose level was assayed on a fasting stomach (basal level) and 30, 60, 90 and 120 min after carbohydrate loads.

Blood glucose level was measured by the glucose oxidase method [8]. The glycemic curves were interpreted according to S. G. Genes [1].

Concurrently, in a homogenate of pancreatic tissue, we evaluated α-amylase activity [5], whereas in a homogenate of the mucosa of the duodenum, proximal and distal small intestine, we examined the level of α-amylase sorbed from pancreatic juice by the small intestine cell surface and intestinal carbohydrases--invertase, maltase and γ-amylase contained in the digestive-transport ensembles of epitheliocytes [3]. The radioimmunoassay method was used to examine blood levels of radioimmune insulin and glucagon with the standard set of reagents.

Tests were performed on 250 animals on the 3d, 7th, 15th, 30th, 60th, 90th and, in a number of instances, the 120th day of restricted motor activity (RMA).

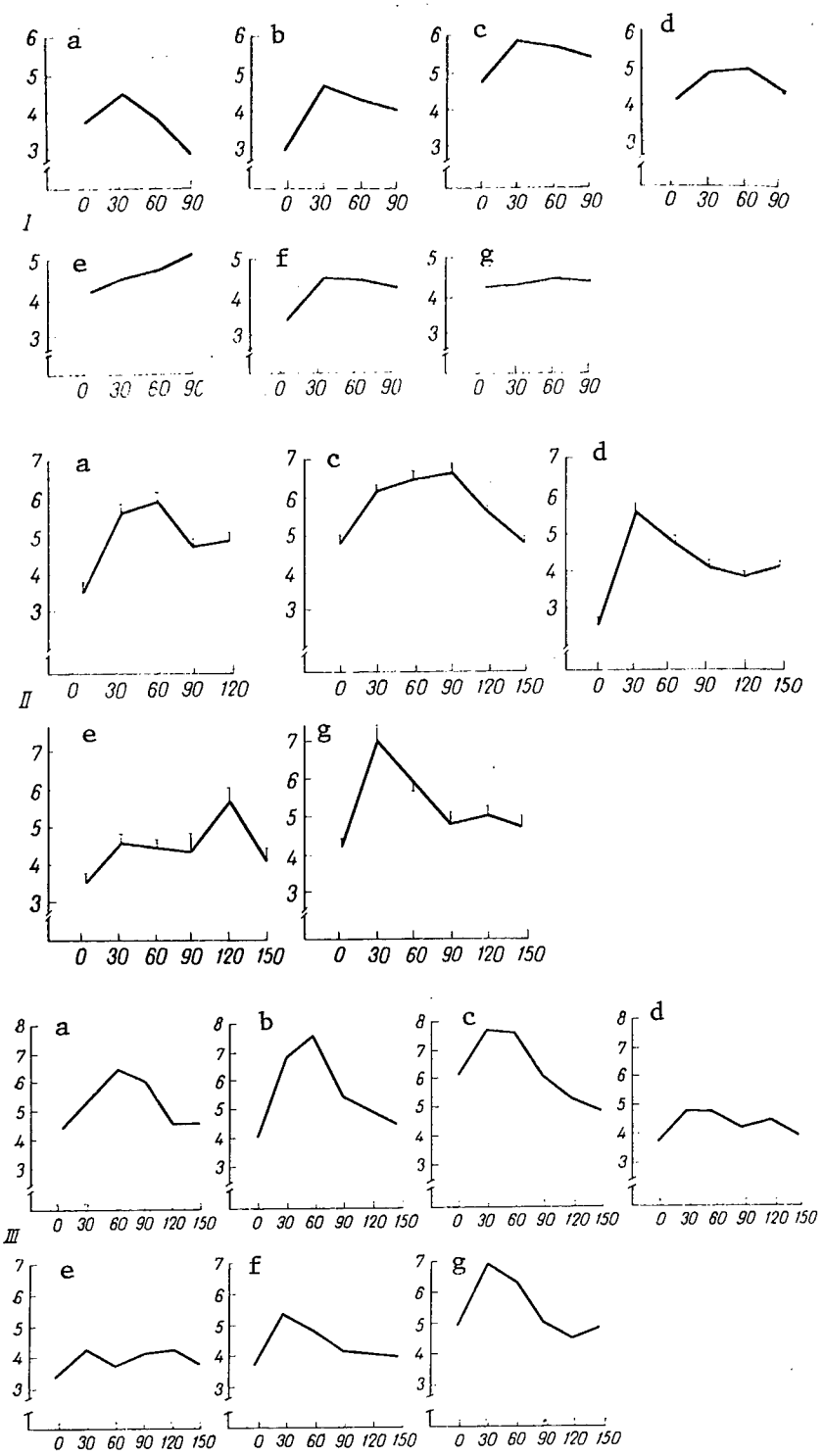

Figure 1. Rats' glycemic curves during restricted motor activity; x-axis, duration of RMA (min)
I, II, III) following starch, maltose and glucose loads, respectively
a) control b-g) 3d, 7th, 15th, 30th, 60th and 90th days of RMA

A comparison was made of the results obtained for experimental and control groups of animals. Reliability of differences between compared parameters was assessed using Student's criterion.

Results and Discussion

1. Functional test with starch load. Figure 1,I illustrates the results of assaying blood glucose level in rats before and after starch load during RMA. Hyperglycemia developed for 15 days of RMA, being the most marked on the 7th day. At this time there was increased hydrolysis of starch in the gastrointestinal tract, and by the 15th day this process slowed down, although there was some increase in glucose utilization. By the 30th day, the basal blood glucose level virtually failed to differ from the preceding tested time, but the glycemic curve acquired a protracted appearance. Maximum increment of glucose was observed 90 min after the load, which was indicative of slower hydrolysis of starch. There was an increase in intensity of glycemia and hyperglycemic ceiling, as compared to the 15th day. On the 60th day of RMA, we observed a decline of basal blood glucose level, which virtually failed to differ from the control. After the starch load, maximum blood glucose increment was high and remained so after 30 min. This is indicative of acceleration and increased efficiency of hydrolysis in the cavity of the gastrointestinal tract, and slowing of the process of glucose utilization. On the 90th day of RMA, the basal blood glucose level rose again, while the glycemic curve was flat, which could be related exclusively to changes in α-amylase activity in the cavity of the gastrointestinal tract.

2. Functional test with maltose load. Figure 2,II illustrates the results of testing blood glucose level in rats before and after functional load with maltose in the course of RMA. In the control group of animals, maximum glucose increment in blood was observed 60 min after the maltose load. On the 7th day of RMA there were higher and flatter glycemic curves than in the control, which is indicative of inhibition of activity of the enzyme-transport systems of the small intestine; however, there was faster utilization of glucose than in the control. On the 15th day of RMA, base level of blood glucose dropped and the glycemic curve became steeper. This is attributable to hydrolysis of maltose and transport of nutrients. The process of glucose utilization was slower.

By the 30th day of RMA the base level of blood glucose rose, while the glycemic curve acquired a flatter and more protracted appearance than on the 7th day. At the late stages of RMA (90th day) basal glucose level was still higher than in the control. The glycemic curve was higher than in the control and at all prior stages of RMA.

Thus, in the course of RMA there is a change in state of the enzyme-transport systems of the small intestine, and a weakening of activity of the digestive-transport conveyer of dimers was observed by the 30th day of RMA. With increase in duration of RMA there was increase in activity of these systems.

3. Functional test with glucose load. In the control group of animals, maximum increment of blood glucose was observed 30 min after the monome load (Figure 3). On the 3d day of RMA there was more intensive glycemia due to some

decline of basal blood glucose level. On the 7th day of RMA there was a taller and flatter glycemic curve. Starting on the 15th day of RMA, there was a phase of low glycemic curves. A plateau was formed between the 30th and 60th days after the load. On the 30th day of RMA, the glycemic curve was just as low as on the 15th day. By the 60th day, there was a tendency toward taller glycemic curves, but the blood basal glucose level remained low. On the 90th day of RMA the glycemic curve was generally taller than at the preceding stage. On the 120th day of RMA we again observed a decline of basal level of blood glucose, while the glycemic curve was more extended than on the 90th day of RMA, as indicated by elevation of the hyperglycemic ceiling.

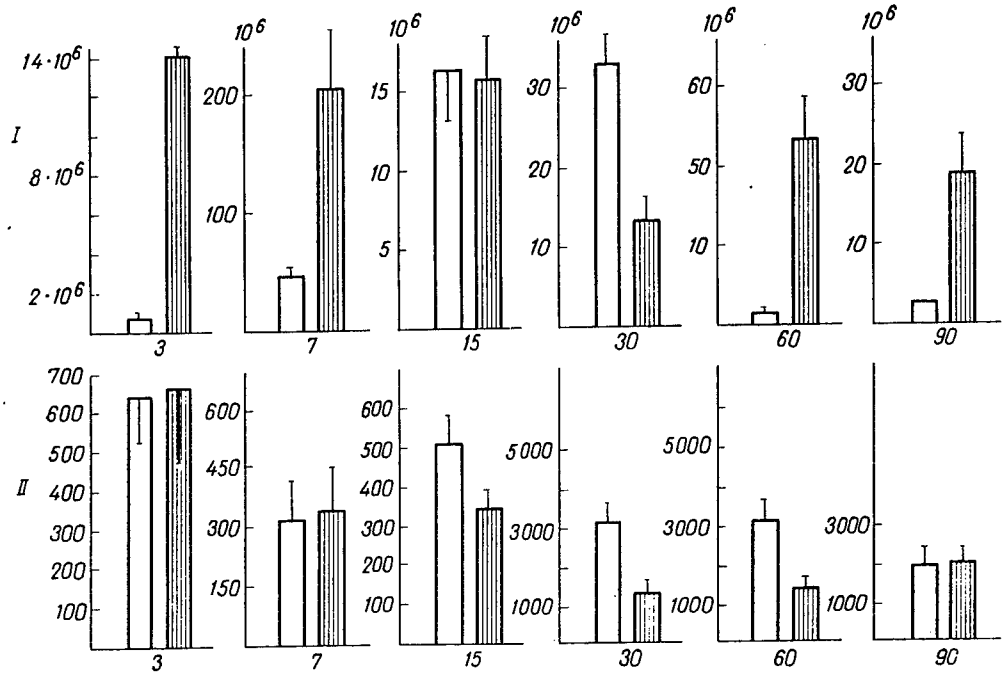

Figure 2. Activity of pancreatic amylase in rats with RMA
I) pancreatic tissue II) duodenal mucosa
X-axis, day of RMA; white bars, control and lined, experiment.

Thus, the functional test with a monomer load enabled us to assess the transport systems of the gastrointestinal tract in the course of RMA. The intensification of monomer transport into the internal environment of the body observed at the early stages of RMA (3 days) was followed by depressed absorption of glucose for 60 days. This was not associated with change in glucose utilization. At later stages of RMA there was intensification of glucose transport and its slower utilization by body tissues.

Figure 2 illustrates the dynamics of α-amylase activity during RMA. At the early stages of RMA (3 days) there was more than 2-fold increase in α-amylase activity in a homogenate of pancreatic tissue. Activity of this enzyme did not change in a homogenate of small intestinal mucosa, whereas the proximal and

distal segments of the small intestine showed a tendency toward increased sorption of α-amylase. By the 7th day of RMA, the elevated level of α-amylase persisted in pancreatic tissue, and it was even higher than on the 3d day; this was associated with virtually no change in amylase incretion. At this time, while amylolytic activity of the duodenal mucosa was unchanged, there was reliable decrease in amylolytic activity of the mucosa of both segments of the small intestine. On the 15th day of RMA, amylolytic activity was normalized in the pancreas and blood. In the small intestine, there was an increase in γ-amylase activity in the proximal segment and decrease in the distal. By the 30th day, there was reliable decrease in amylase activity in the pancreas. The duodenal mucosa showed a reliable decline of amylolytic activity. In the proximal segment of the small intestine, sorption of the enzyme did not differ from the control, whereas in the distal segment it increased reliably. On the 60th day of RMA,there was reliable increase in amylolytic activity of pancreatic tissue. The blood showed a persisting low level of amylase. In the mucosa of the duodenum and proximal segment of the small intestine, amylolytic activity did not differ from the control, but it was somewhat diminished in the distal segment. On the 90th day of RMA, we observed some stabilization of changes in production and incretion of α-amylase, which retained the same direction of changes as on the 60th day. Activity of the enzyme reverted to normal in the duodenum and distal segment of the small intestine, but sorption of amylase was diminished in the proximal segment.

The results of analyzing the carbohydrase spectrum of the small intestine during RMA are illustrated in Figure 3. On the 3d day of RMA, there was a decline of γ-amylase level, which was more marked in the distal segment. Changes in an analogous direction were noted with regard to invertase. On the 7th day of RMA, high γ-amylase activity persisted in both segments of the small intestine, whereas invertase and maltase activity of the small intestine increased. On the 15th day of RMA, there was reliable decrease in activity of maltase in the proximal segment of the small intestine with virtually no changes in invertase activity. By the 30th day of RMA, there was an increase in invertase activity of the small intestine. Maltase activity did not differ from the control. On the 60th day of RMA there was a tendency toward increase in γ-amylase in the proximal segment and decrease in the distal segment of the small intestine. Activity of invertase in both segments virtually failed to differ from the control, while maltase activity diminished reliably. The 90th day of RMA was characterized by reliable increase in glucoamylase activity in both segments of the small intestine. There were no changes in invertase and maltase activity in the proximal segment, whereas in the distal segment there was increase in invertase activity and decrease in maltase activity.

Examination of the endocrine part of the pancreas in the course of RMA revealed different correlations between insulin and glucagon levels. The early stages of RMA were characterized by marked hyperglucagonemia. On the 30th day of RMA there was some hyperinsulinemia and moderate hyperglucagonemia. With longer RMA the basal insulin level remained low, while the stimulated level reverted to control values. The hyperglucagonemia demonstrated at this time was less marked than at the earlier stages.

Thus, in the course of RMA there were dissimilar changes in hydrolysis, transport and utilization of carbohydrates. At the early stages, intensification of carbohydrase activity, which effects cavitary and membrane hydrolysis of

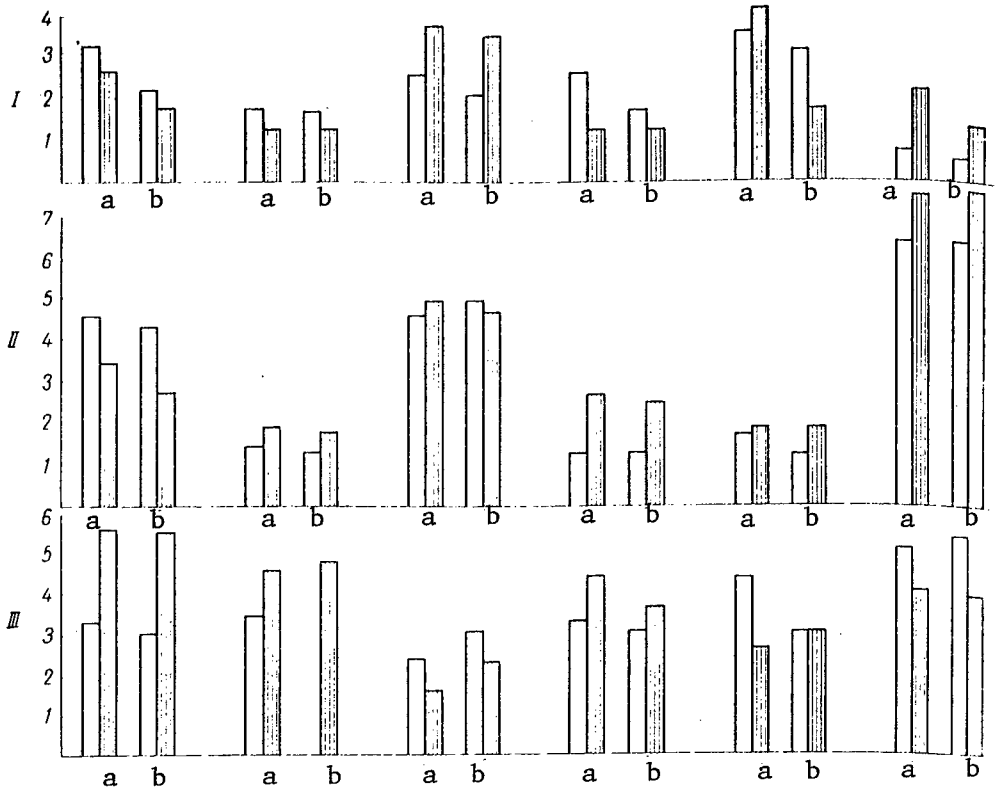

Figure 3. Carbohydrase spectrum of rat small intestine during RMA; white bars, control and lined ones, experiment.

I) α-amylase
II) invertase
III) maltase

a) proximal segment
b) distal segment

carbohydrates, was associated with hyperglycemia and rapid utilization of carbohydrates. This is related to nonspecific reactions under the effect of RMA, when the body has an increased requirement for energy substrate [2, 4, 9]. By the 30th day of RMA, there is depression of the system of hydrolysis and transport of carbohydrates, development of hypoglycemia, but utilization of glucose is not impaired. At this time, there is less intensive carbohydrate metabolism via the glycolytic and, particularly, oxidative pathways, and an increase in sensitivity to insulin [7]. At the later stages of RMA, there is development of adaptive reactions by the carbohydrate hydrolysis and transport systems; depression of pancreatic amylase is associated with some activation of enzyme-transport systems of the small intestine and resorption of glucose. The glycemic curves acquire an extended appearance, which is indicative of slower utilization of glucose. This is attributable to changes in the endocrine part of the pancreas. Imbalance of systems responsible for glucose homeostasis prevents the normal course of glucose utilization. For this reason, the body tries to provide for passage of glucose into tissues and raise its concentration in blood. Activation of pancreatic amylase in blood and intestinal disaccharidases is one way of increasing passage of glucose into blood.

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POSSIBILITY OF PHARMACOLOGICAL CORRECTION OF REGIONAL OSTEOPOROSIS IN NONBEARING EXTREMITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 18 Oct 85) pp 47-51

[Article by I. V. Rogacheva, A. N. Polyakov, A. I. Volozhin and G. P. Stupakov]

[English abstract from source] In 20- and 40-day rat studies the prophylactic effect of retabolil and calcitrin (calcitonin) against hypodynamics-induced osteoporosis was investigated. Hypodynamics was produced by surgical amputation of the lower third of the leg and hence by loss of the support function of the limb. Retabolil was injected intramuscularly at a dose of 0.2 ml once a day for 10 days and calcitrin was injected subcutaneously at a dose of 2 units MRC in 0.5 ml distilled water once a day. The results indicate that osteoporosis in the supportless bone of the experimental animals and that seen during space flight developed in a similar way. In the experiment retabolil and calcitrin inhibited the progressive development of osteoporosis but the strongest effect was obtained upon a combined application of the two drugs.

[Text] A number of authors have tried to attenuate the adverse effects of long-term restriction of motor activity on animal bones using hormones--calcitonin and somatotropic hormone [1-3]. In these studies, experimental models were used, in which animals were kept in tight cages that limited their motor activity drastically, but with retention ofbearing function of the limb. At the same time, hypodynamia, due to removal of load on the skeletomuscular system, is the main factor affecting the skeletal bones during actual spaceflights. We have determined that the nonbearing position of a limb following amputation of the lower leg is an adequate model of the hypodynamia caused by weightlessness, since development of osteoporosis, change in element composition of bone tissue and its strength properties were analogous under these conditions [8]. To date, no studies had been made of the efficacy of agents that normalize bone metabolism with simulation of weightlessness, and for this reason we undertook this investigation.

Methods

The studies were conducted on 150 Wistar rats with a base weight of 180-200 g. Hypodynamia was produced by amputation of the crus in the region of the lower

third under ether anesthesia. After the operation, the animals were divided into four groups: the 1st consisted of rats given no preventive agents (control); the 2d, animals given calcitrin (at the rate of 2 MRC units (Footnote)(The standard was elaborated in 1965 in the department of biological standards of the London National Institute of Medical Research) in 0.5 mℓ distilled water, subcutaneously every other day); the 3d group consisted of animals given retabolil (0.2 mℓ, once every 10 days intramuscularly), and the 4th, rats given calcitrin with retabolil in the same dosage. The agents were given to the animals for 20 and 40 days. The rats were sacrificed using ether, their femurs were isolated, fixed in 0.5% neutral formalin and stored under refrigeration until needed. Determination was made of weight and volume of the entire bone, head and distal epiphysis, as well as density, ash and mineral content. Thickness of the cortical layer and width of the bone marrow canal were determined on frontal and lateral x-ray projections. The methods have been described previously [3]. Histological transverse sections of the femoral diaphysis were prepared from the femoral bone fragments (from 3 animals in each group). The preparations were stained with hematoxylin, eosin and according to van Gieson. Mineralization of bone microstructures was evaluated by the method of quantitative contact microroentgenography of cross-sections, determining mineralization of 20-30 points on each microroentgenogram. Cross-sections of the femoral diaphysis were used for microroentgenography, and mineralization of microstructures was determined over the entire width of the cortical layer in 30 animals used in the 20-day experiment and 32 in the 40-day experiment. Each pair of microroentgenograms of cross-sections of both femurs from the same animal was evaluated according to mean mineralization of microstrcutures in the experiment and control. To assess the effect of the hormones used on femoral bone tissue of the nonbearing limb, data obtained from examining the femur of the nonbearing limb of rats in the 1st group served as the control. The results of examining the femur of the bearing limb of rats in the 2d-4th groups were compared to the corresponding parameters for the bearing limb of rats in the 1st group in order to determine the effect of the hormones on normal bone. All digital data obtained in the course of this study were submitted to statistical processing.

Results and Discussion

As a result of 20- and 40-day hypodynamia, there was a decrease in thickness of the cortical layer of the femoral diaphysis in the nonbearing limb of rats in the 1st group, more so in the frontal projection than the lateral, without noticeable increase in width of the medullary canal (Table 1), which is consistent with previously published data [6]. As a result, the "nonbearing" bone was lighter than the "bearing" one due to decrease in weight of the distal epiphysis, head and diaphysial part. Density of the spongiosa of the femor of the nonbearing limb (head, distal epiphysis) was considerably lower on the 20th day of the experiment than in the bearing limb (Table 2). The decrease in mineralization refelcted development of osteoporosis and a minor decrease in mineralization of organic matter (ash content) of bone tissue, and the changes in the head were less marked, corresponding to those found in rats following a 20-day spaceflight [5, 7], which characterizes the adequacy of the chosen model of weightlessness.

Table 1. Changes in transverse dimensions (mm) of femoral diaphyses of nonbearing limb of rats under the effect of calcitrin and retabolil

Exper. day	Parameter	Animal group								
		2d control (bearing limb)	1st	% of bearing side	2d	% of control	3d	% of control	4th	% of control
20	Thickness of cortical layer	1,14±0,03	1,05±0,02	92,1*	0,94±0,03	89,5*	0,84±0,03	80,0*	0,93±0,05	88,6*
	Diaphysis width	3,48±0,05	3,37±0,06	96,8*	3,22±0,04	95,5	3,28±0,09	97,3	3,24±0,07	96,1
	Width of medullary canal	2,29±0,07	2,29±0,08	100,0	2,24±0,06	97,8	2,06±0,02	89,9*	2,36±0,04	103,0
40	Thickness of cortical layer	1,11±0,05	0,96±0,02	86,5*	0,96±0,06	100,0	0,84±0,03	88,0	0,92±0,05	95,8
	Diaphysis width	3,45±0,08	3,26±0,06	94,5	3,08±0,04	94,7*	3,28±0,09	100,6	3,34±0,07	102,5
	Width of medullary canal	2,36±0,04	2,27±0,05	96,2	2,25±0,04	99,2	3,06±0,02	90,7	2,32±0,07	102,5

Note: Here and in Table 2, the asterisk indicates that differences are reliable.

Table 2. Changes in mineralization (g/cm^3), density (g/cm^3) and ash content (%) of fragments of nonbearing rat femur under the effect of calcitrin and retabolil

Exper. day	Parameter	Femoral fragment	Animal group								
			2d control (bearing limb)	1st	% of bearing side	2d	% of control	3d	% of contr.	4th	% of contr.
20	Mineralization	Head	0,587±0,01	0,436±0,02	74,3*	0,466±0,03	106,9	0,409±0,02	93,8	0,463±0,03	106,2
		Distal ep.	0,430±0,02	0,298±0,02	69,3*	0,283±0,01	95,0	0,304±0,02	102,0	0,343±0,02	115,1
	Density	Head	1,018±0,02	0,709±0,07	77,6*	0,862±0,03	121,6	0,780±0,03	110,0	0,855±0,03	120,6
		Distal ep.	0,792±0,02	0,611±0,01	77,1*	0,578±0,02	95,6	0,662±0,02	108,3	0,662±0,02	108,3*
	Ash content	Head	0,567±0,02	0,557±0,01	98,2	0,540±0,02	96,9	0,491±0,01	88,1*	0,544±0,01	97,7
		Distal ep.	0,563±0,02	0,478±0,01	84,9*	0,483±0,01	101,0	0,457±0,01	95,6	0,516±0,01	107,9*
40	Mineral.	Head	0,586±0,02	0,479±0,02	81,7*	0,587±0,04	122,5*	0,536±0,03	111,9	0,537±0,03	112,1
		Distal ep.	0,420±0,02	0,330±0,02	78,6*	0,358±0,03	108,5	0,327±0,02	99,1	0,381±0,02	115,4
	Density	Head	1,009±0,01	0,885±0,03	87,7*	1,018±0,03	115,0*	0,875±0,02	98,9	0,908±0,02	102,6
		Distal ep.	0,772±0,04	0,648±0,03	83,9*	0,707±0,03	109,7	0,643±0,02	99,2	0,731±0,04	112,8
	Ash	Head	0,586±0,02	0,540±0,07	92,1	0,569±0,01	105,4	0,579±0,02	98,8	0,576±0,02	106,7
		Distal ep.	0,538±0,02	0,522±0,07	97,0	0,555±0,01	106,3	0,499±0,01	95,6	0,523±0,07	100,2

Key: ep) epiphysis

The analogous parameters for the head and distal epiphysis in the nonbearing limb presented the same direction in the 40-day experiment, but they were less changed. At both observation periods, no corresponding changes were demonstrable in the femoral diaphysis of experimental animals.

Histological sections of the femoral diaphysis on the nonbearing side showed porosity of bone after 20-day hypodynamia, manifested by increase in diameter of haversian canals, narrowing of cortical layer, discontinuity and unevenness of the layer of external general plates. Some preparations of the femoral diaphysis on the bearing side also presented areas of cortical bone with dilated haversian canals. After 40-day hypodynamia, histological preparations of bone revealed a decrease in porosity of cortical plates. The smaller width of the cortical plate on the nonbearing side was indicative of depression of osteogenetic processes in the absence of static load on the limb.

Table 3. Mineralization (g/cm^3) of microstructures of the femoral diaphysis of nonbearing limb under the effect of calcitrin and retabolil (20- and 40-day hypokinesia)

Specimen No	Group 1		2		3		4	
	nonbearing [nb]	bearing	nb	bearing	nb	bearing	nb	bearing
	20-day hypokinesia							
1	1,25±0,01	1,25±0,01	1,40±0,01	1,39±0,01	1,39±0,01	1,30±0,01	1,30±0,01	1,37±0,02
2	1,39±0,02	1,38±0,03	1,30±0,02	1,38±0,02	1,37±0,02	1,37±0,01	1,39±0,02	1,37±0,01
3	1,37±0,01	1,35±0,02	1,31±0,02	1,30±0,02	1,43±0,02	1,42±0,01	1,36±0,02	—
4	1,33±0,01	1,35±0,02	1,34±0,02	1,35±0,01	1,28±0,01	1,36±0,01	1,31±0,02	1,37±0,02
5	1,33±0,01	1,36±0,05	1,34±0,01	1,31±0,01	0,32±0,03	1,34±0,02	1,33±0,02	1,30±0,04
6	1,36±0,02	1,33±0,01	1,34±0,02	1,37±0,01	1,38±0,02	1,33±0,02	1,33±0,02	1,33±0,01
7	1,36±0,01	1,36±0,01	1,32±0,02	1,32±0,03	1,32±0,01	1,33±0,01	1,23±0,02	1,33±0,02
8	1,33±0,02	1,29±0,02	—	1,34±0,02	—	—	—	—
	40-day hypokinesia							
1	1,44±0,01	1,31±0,04	1,29±0,01	1,17±0,01	1,27±0,01	1,25±0,02	1,23±0,02	1,13±0,01
2	1,10±0,02	1,25±0,02	1,13±0,01	1,12±0,02	1,29±0,02	1,24±0,01	1,36±0,01	1,33±0,01
3	1,26±0,01	1,25±0,02	1,25±0,01	1,21±0,02	1,32±0,02	1,40±0,01	1,21±0,01	1,31±0,01
4	1,27±0,02	1,24±0,01	1,20±0,02	1,10±0,01	1,40±0,01	1,42±0,01	1,19±0,01	1,30±0,03
5	1,28±0,04	1,29±0,03	1,31±0,02	1,29±0,01	1,31±0,01	1,26±0,01	1,37±0,01	1,34±0,01
6	1,35±0,01	1,33±0,01	1,23±0,02	1,23±0,02	1,23±0,01	1,28±0,01	1,30±0,03	1,28±0,01
7	1,21±0,02	1,28±0,01	—	1,11±0,02	1,29±0,01	1,18±0,04	1,17±0,01	—
8	1,40±0,02	1,38±0,01	1,32±0,01	1,30±0,03	1,31±0,02	1,30±0,03	1,28±0,01	1,16±0,01

Mean levels of mineralization of bone microsctructures on the nonbearing side were the same in the 2-day experiment as on the bearing side (Table 3). In the experiment with 40-day hypodynamia, like the 20-day experiment, there were no appreciable differences between mineralization of microstructures on the operated side and symmetrical bone (see Table 3). Mean levels of microstructure mineralization for the two periods (20 and 40 days) were essentially the same.

Injection of calcitrin for 20 days, and particularly for 40 days, led to increase in density and mineralization of the head of the femur on the nonbearing side, as compared to the control, mainly due to increased mineralization of organic matter (ash content). Rats given calcitrin revealed, on the 20th day, a decrease in thickness of cortical layer of femoral diaphysis in frontal and lateral projections, by a mean of 8-9%, as compared to the appropriate control. By the 40th day there was no manifestation of this difference.

Analysis of microroentgenographic data on the 40th experimental day revealed that use of calcitrin as a preventive agent had no effect on level of mineralization of microstrcutres. Osteoporosis was less marked in the cortical layer on microroentgenograms and histological preparations.

Use of retabolil alone for 20 days led to unreliable increase in density of the head and distal epiphysis of the femur on the nonbearing side. In the 40-day experiment this effect was not observed. The 3d group of animals presented a greater decrease in thickness of the cortical layer than the 2d group. According to the results of histological examination of the preparations, there was a decrease in osteoporotic thinning of the cortical plate of the femoral diaphysis. Injections of retabolil did not have an appreciable effect on mineralization of diaphysial microstructures on the nonbearing and bearing sides, according to microroentgenography, but did result in a distinct tendency toward decrease in ash content of spongy structures.

Injection of calcitrin together with retabolil led to increase in density and mineralization of the head and distal femoral epiphysis on the nonbearing side at both tested times. There was also increase in mineralization of bone diaphysis on the 40th experimental day. The effect of the agents is attributable to normalization of mineralization of organic matter, as indicated by the increase in ash content of spongiosa. Osteometric parameters of the femoral diaphysis were characterized by a smaller thickness of the cortical layer 20 days after the start of the experiment, but only in the frontal projection. No changes were noted on the 40th day.

Use of either retabolil alone or in combination with calcitrin had no effect on mean mineralization of microstructures of diaphysial bone tissue. According to the results of histological examination and evaluation of microroentgenograms, combined use of calcitonin and retabolil had the most stable preventive effect on development of osteoporosis of all the variants used. This was associated with increase in density of structures, and we observed a tendency toward normalization of their mineralization.

With reference to our findings, it must be noted that removal of static load on a limb by rendering it nonbearing (amputation) is an adequate experimental model of osteoporosis that occurs during spaceflights and long-term bedrest of patients. It must be assumed that, under these model conditions, there were no systemic changes in neurohumoral regulation of phosphorus and calcium metabolism, while osteoporosis was caused by local conditions--hypodynamia and hypokinesia--which led to local change in trophic conditions and, accordingly, to regional structural impairment of bone tissue. It is also possible that, in the absence of a static load, there was a change in reactivity of tissue to the most important regulators of bone metabolism. This hypothesis is indirectly confirmed by the results of our investigation, in which administration of calcitrin and retabolil had a preventive effect on osteoporosis occurring as a result of hypodynamia.

The greater "requirement" of bone for protein metabolism stimulators could be attributed to a set of factors, including decrease in reactivity of osteocytes to adequate regulators of their functions, in the presence of impairment of microcirculatory processes that are always associated with hypodynamia.

The response obtained from use of calcitrin and retabolil for osteoporosis occurring as a result of hypodynamia enables us to pursue further investigations in this direction, in order to find the optimum variant of pharmacological treatment of development of osteoporosis.

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MORPHOLOGICAL AND BIOCHEMICAL ANALYSIS OF SOME RAT ORGANS AND TISSUES FOLLOWING EXPOSURE TO 1.1 and 2.0 G GRAVITY

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[Article by I. B. Krasnov, I. I. Babichenko, B. V. Afonin and A. S. Pankova]

[English abstract from source] During 30 days rats were centrifuged at 1.1 and 2.0 G. On centrifugation day 30 the rats showed body mass losses, decrease of plasma ACTH, activation of the renin-angiotensin-aldosterone system (RAAS) and ultrastructural changes in the mossy fiber terminals in the nodulus cortex which were indicative of the state of excitation (at 1.1 G) or excess excitation (at 2.0 G) in the system of the utriculus receptor cell and vestibular ganglion neuron (RCN). On the 2d day after centrifugation the ultrastructural changes in the terminals pointed to a lower activity of the RCN system which was below the physiological norm. As compared to centrifugation day 30, the RAAS became more active on the 2d day of recovery. On the 7th day of recovery (after centrifugation at 1.1 G) the RCN ultrastructure, RAAS and ACTH concentrations returned to the normal. The general trends of the RAAS and RCN changes seen on the 2d day of recovery and identified by other authors at an acute stage of adaptation to microgravity suggest that the data obtained on the 2d day of recovery may be used to analyze certain effects which develop during an acute stage of adaptation to microgravity in mammalian organs and systems responsible for the perception of modified gravity and their adaptation to a new level of gravity.

[Text] It is impossible to reproduce on earth a state of wieghtlessness in mammals for several hours and days. The existing experimental models make it possible merely to obtain some of the physiological effects of weightlessness, but they do not produce weightlessness or hypogravity for the entire body, and they do not attenuate the effect of earth's gravity on the otolith system. At the same time, it is possible to produce relative hypogravity (RHG) on earth by eliminating the effect of hypergravity (HG), to which an organism has been adapted by, for example, rotation on a centrifuge [22]. Apparently, the first stage of adaptation to RHG must correspond to the acute period of adaptation to weightlessness, according to the direction of changes in organs and systems related to perception of changes in gravity with adaptation to a new level of

the latter. To check this hypothesis, we conducted experiments on rats to test the effect of 30-day HG (exposure to accelerations of 1.1 and 2.0 G) and 2-7-day RHG on weight of the body, adrenals and thymus, levels of some blood plasma hormones, as well as state of ultrastructure of the cerebellar nodulus cortex at the sites of the endings of primary vestibular fibers carrying information from receptor cells of the otolith system (Footnote 1)(This study is a portion of investigations of effects of hypergravity on animals [6]).

Methods

Hypergravity was produced by rotating animals on a centrifuge for 30 days. Male SPF rats (80 days old and weighing 259 g at the start of the experiment) were kept in unrestricted groups of 10 per cage (or centrifuge compartment), and they were divided into 3 equal groups: one group was in the peripheral compartments of the centrifuge (P group), another in the central compartments (C group) and the third, in ordinary cages away from the centriuge (control--K group). The centrifuge, with a 141-cm radius for the peripheral compartment, was rotated at the rate of 33.3 r/min. Gravity levels were 2.0 and 1.1 G in the peripheral and central compartments, respectively. All of the animals were in the same room with a 12:12 h ratio between daylight and darkness, and they were kept on a similar diet. The centrifuge was stopped for 1 h at the same time of day to fill the water bottles and feeders, and to clean the cages daily. On the 30th day of rotation and on the 2d and 7th days after 30-day rotation (2d and 7th day of RHG), we weighed the animals and decapitated them. We examined seven rats from each group. For electron microscopy, nodulus fragments taken from the left half of the cerebellar vermis were fixed by immersion in 2.5% glutaraldehyde solution in 0.1 M phosphate buffer, pH 7.4, with additional fixing in 1% osmium tetroxide in the same buffer, and imbedded in araldite. Ultrafine sections were examined under a TESLA-BS-500 electron microscope. Concentration of adrenocorticotropic hormone (ACTH), as well as angiotensin I and aldosterone and renin activity--which are elements of the renin-angiotensin-aldosterone system (RAAS)--in mixed blood plasma were assayed by the radioimmune method. After weighing the thymus and adrenals, the latter were fixed in Bouin fluid, imbedded in paraffin, and 10-μm sections were stained with eosin and hematoxylin.

Results and Discussion

Macroscopic examination of the brain, thoracic and abdominal organs of rats failed to reveal any pathological changes. On the 30th day of HG, P and C groups of rats showed a tendency toward reduction of weight, which was more marked in the P group (Table 1). On the 2d day of RHG, weight of P group rats was reliably reduced, as compared to C and K groups, by 9.7 and 13.4%, respectively (Table 1), but in comparison to the 30th day of HG it showed virtually no change, whereas in the C group, weight increased by 4.7%, as compared to the 30th day of HG (see Table 1). On the 7th day of RHG, rats in C and P groups continued to present a lower weight than K group animals, although the rate of its positive change was virtually the same, as compared to the 30th day of HG (7.7 and 5.9%). The tendency toward decrease in weight on the 30th day of HG is confirmed by data on the inhibitory effect of HG on growth of mice [17, 26], hamsters [27], rats [9, 20] and chicks [22]. On the 30th day of HG, absolute and relative weight of the thymus and adrenals of P and C groups of rats showed virtually no difference from that of K group rats, and it did not change

appreciably on the 2d and 7th day of RHG (Table 2), which confirms the data obtained after exposing rats to 2.1 G for 28 days [9]. The normal morphological structure of individual zones of he adrenal cortex and their clearcut boundaries in group P and C rats on the 30th day of HG and 2d and 7th days of RHG, as well as absence of changes in weight of the adrenals and thymus, are indicative of both animal adaptation to HG, which occurred on the 30th day of rotation on the centrifuge, and absence of stress reaction to RHG [9].

Table 1. Rat weight and changes after exposure to HG and RHG (M±m)

Animal group	Body weight, g (M±m)				Wt. change as compared to 30th day of HG, %	
	0 day of experim.	30th d of HG	2d day of RHG	7th day RHG	2d d of RHG	7th day of RHG
K	259,4±3,0	302,8±8,3	314,3±12,8	333,0±17,1	+3,8	+10,0
C	259,1±3,5	287,8±6,8	301,4±6,8	310,0±6,2	+4,7	+7,7
P	258,0±2,4	275,1±3,9 (—9,3*,—4,6)	272,1±6,2 (—13,4*,—9,7*)	291,4±6,0 (—12,5,6,0)	—1,1	+5,9

Note: Changes (%) in mass and relative parameter for K and C groups, respectively, are shown in parentheses. Asterisk indicates $P<0.05$.

Table 2. Weight of rat thymus and adrenals after HG and RHG (M±m)

Organ	Group	Absolute weight, mg			Relative wt., mg/100 g body wt.		
		30th d of HG	2d day of RHG	7th d of RHG	30th d of HG	2d day of RHG	7th day of RHG
Thymus	K	257±25	218±10	212±19	84,3±6,2	69,4±2,4	64,5±6,0
	C	224±24	225±17	216±12	74,4±8,2	74,5±5,3	69,8±5,3
	P	228±31	197±9	217±17	79,9±9,3	71,0±4,7	74,3±5,4
Adrenals	K	36,3±1,5	37,9±1,0	39,8±2,1	12,0±0,1	12,0±0,1	11,9±0,5
	C	38,1±2,3	38,0±1,3	39,8±2,8	13,1±0,5	13,0±0,4*	12,7±0,7
	P	36,3±1,5	36,7±1,9	35,0±1,7	12,9±0,4	13,0±1,0	12,0±0,4

Note: Asterisk indicates $P<0.05$, as compared to parameters for the K group.

On the 30th day of HG, ACTH concentration in plasma was equally reduced in C and P groups of animals (Table 3). But, while ACTH concentration reverted to normal on the 7th day of RHG in group C, where rats were exposed to 1.1 G, in the P group, which was exposed to 2.0 G, ACTH concentration remained low on the 7th day of RHG. While depression of ACTH secretion was obviously a function of level of gravity, the mechanism of this depression is still unclear. One of the causes of this phenomenon could have been appearance of a static focus of excitation in the hippocampus upon stimulation of the vestibular system [11], which may have a depressing effect on ACTH secretion [13]; another cause, is the possible effect (via a feedback mechanism) of high glucocorticoid levels in blood, intensified secretion of which by the adrenals could apparently still occur after changing from HG to RHG, in spite of disappearance of an increased glucocorticoid requirement of tissues, which occurred during adaptation to HG.

Table 3. Activity of renin, concentration of angiotensin I, aldosterone and ACTH in mixed blood plasma of rats submitted to HG and RHG (M±M)

Hormone	Group	Stage of experiment		
		30th d of HG	2d d of RHG	7th d of RHG
Renin, ng/mℓ/h	K	0,600±0,09	0,663±0,07	0,706±0,04
	C	0,603±0,08	0,826±0,12*	0,750±0,05
	P	0,797±0,10	0,906±0,11*	0,700±0,06
Angiotensin I, pg/mℓ	K	137,0±26,5	186,0±44,6	126,0±28,7
	C	206,0±27,9	526,0±64,2*	98,0±19,2
	P	365,0±39,1*	546,0±59,9*	162,0±67,0
Aldosterone, pg/mℓ	K	87,4±14,0	83,1±12,9	92,5±16,5
	C	95,9±15,5	188,8±10,6*	122,2±12,6
	P	125,1±15,5*	247,6±40,7**	125,7±30,5
ACTH, pg/mℓ	K	158,4±38,4	149,8±48,0	115,0±64,2
	C	59,5±22,3*	75,9±11,8	133,0±61,4
	P	51,9±21,1*	42,6±8,7*	49,0±21,7*

*P< 0.05, as compared to control parameters.
**P< 0.01.

In the P group of rats submitted to HG for 30 days, we observed activation of RAAS in blood plasma, which was generally similar to activation of this system in man when exposed to brief accelerations [1], but at the same time it differed in that there was insignificant increase in activity of renin, which is the triggering element of the RAAS (see Table 3). On the 2d day of RHG, C and P group rats presented activation of RAAS, as compared to the K group, and it was more marked in the P group. The increase in RAAS activity was also demonstrable in comparison to the 30th day of HG, and the activity of the first elements of this hormonal system was more marked in the C group, while the concentration of aldosterone--the last element in the system--increased equally in P and C group animals. This activation of RAAS can be compared to the increase in aldosterone content of human plasma in the acute period of adaptation to weightlessness [18] or hypokinesia with the head tilted down [19], and it is apparently unrelated to stress, apparently being a secondary factor. The signs of RAAS activation become less apparent on the 7th day of RHG in both group C and P animals, perhaps due to completion of the process of adaptation to earth's gravity.

Examination of ultrastructure of the granular layer of the cerebellar nodulus cortex in group K rats revealed that the terminals of moss fibers (TMF) are situated in the central part of glomerules, contain synaptic vesicles (SV) grouped in the synaptic region and intact mitochondria with electron-dense matrix and numerous cristae. The synaptic contacts between TMF and dendrites of granule-cells have an asymmetrical type of strucutre and consist of two electron-dense membranes and postsynaptic induration. The postsynaptic profiles of granule-cell dendrites usually contain one mitochondrium with electron-dense matrix and flat cisterna next to it. The granule-cells situated around glomerules have a round nucleus with peripheral location of chromatin and a narrow perinuclear space, in which there are free ribosomes, mitochondria and a laminar complex represented by flat cisternae and a small number of vesicles (Figure 1).

The TMF and granule-cells of rats in group C, submitted for 30 days to HG (1.1 G) there were ultrastructural changes indicative of excitation. The TMF revealed

increase in number of SV in the region of synaptic contacts, as well as in number of fimbriated and large clear vesicles, high electron density of pre- and postsynaptic membranes and postsynaptic induration [8], increased width of synaptic cleft and electron density of its matrix [3]. Clearing of the matrix and shortening of mitochondrial cristae are also observed (Figure 2). There was an increase in length of cisternae in postsynaptic elements of synaptic contacts. The granule-cells showed an increase in area of chromatin condensation in the nucleus, widening of the perinuclear space, dilatation of laminar complex and increase in number of free ribisomes, which were indicative of excitation of these cells [7].

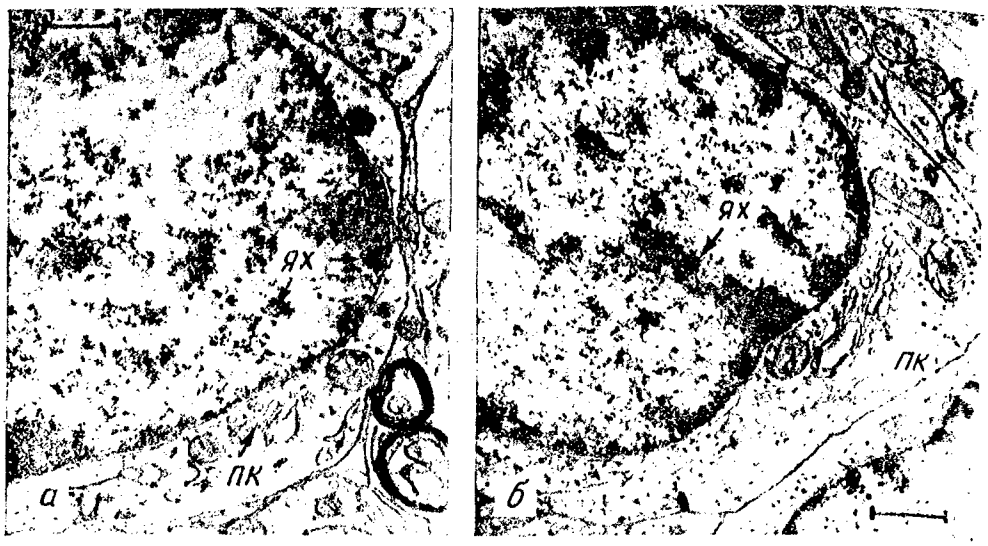

Figure 1. Granular cell of rat cerebellum nodular cortex

a) granular cell of vivarium control rat; activity is within the physiological norm; magnification 16,000×; scale 0.625 μm
b) granular cell from rat submitted to 2.0 G for 30 days; excitation; magnification 16,000×; scale 0.625 μm
ПК) laminar complex
ЯХ) nuclear chromatin

TMF structure changed in 3 directions in P group rats on the 30th day of HG (2.0 G). In some terminals the ultrastructure was typical of excessive excitation [3] leading, in a number of instances, to blocking of synaptic transmission: dramatic increase in density of SV in TMF, many fimbriated vesciles, most mitochondria contain clear spaces and altered cristae, there are presynaptic zones without a marked concentration of SV. In some synapses, the SV are 8-10 nm away from the presynaptic membrane, the synaptic cleft is not dilated, electron density of synaptic membranes is reduced, which is indicative of blocking of synaptic transmission [5, 21, 25]. Mitochondria of postsynaptic elements adjacent to TMF have a cleared matrix, shortened cristae, and they are usually surrounded by two postsynaptic cisternae, which is indicative of increased functional activity of these elements. The ultrastructure of another part of the TMF resembles the "light" type of degeneration [4, 12, 14, 23]: axoplasm is

cleared, there is a smaller total number of SV, which form groups of 8-12 andic are 8-12 nm away from the presynaptic membrane over a considerable part of its length, and the central part of TMF is occupied by altered mitochondria. In the third group, TMF, the ultrastructure of which resembles the "dark" type of degeneration [4, 14, 23], show an increase in electron density of axoplasm due to more compact arrangement of SV (Figure 3). There are mitochondria with electron-clear matrix and shortened cristae in the central parts of such TMF. Sunaptic contacts are in an inactive state: the matrix of the synaptic cleft is electron-clear and postsynaptic induration is not enlarged. The postsynaptic structures adjacent to presynaptic elements of terminals with "light" and "dark" axoplasms contain mitochondria with vacuoles and destroyed cristae, as well as dilated, fragmented postsynaptic cisternae, which is indicative of dramatic decrease in their functional activity [2, 16]. Granular cells of group P rats are characterized by dilated perinuclear space, in which there are grouped ribosomes, widened laminar complex and drastically vacuolized cisternae. However, the density of distribution of chromatin along the periphery of the nucleus is low, which is indicative of less marked excitation of these cells than the granular cells of group C rats on the 30th day of HG.

Since the ultrastructure of TMF reflects the level of functional activity of neurons of vestibular ganglion, which receive information from receptor cells of the otolith system, our findings warrant the conclusion that 30-day exposure to 1.1 G elicits a state of excitation in the system of the utricular receptor cell--neuron of vestibular ganglion, while 30-day exposure to 2.0 G elicits a state of hyperexcitation. The ultrastructural changes in TMF of rats in the P group, which resemble TMF regeneration of the "light" or "dark" type, are apparently due to the prolonged and intense excitation of vestibular ganglion neurons as a result of stimulation of otolith receptor cells under the effect of 2.0 G, and they apparently constitute the next stage of changes in TMF ultrastructure following hyperexcitation demonstrated in some TMF of the same group of rats.

On the 2d day of RHG, group C rats showed changes in ultrastructure of TMF and granular cells indicative of decline (below the normal level) of intensity of synaptic transmission [24]. The TMF axoplasm contains few SV which, in rare instances and in small number, are grouped near synaptic contacts, as well as intact mitochondria and mitochondria with electron-dense matrix and a single focus of clearing. In most synaptic contacts, the matrix of the synaptic cleft is electron-clear and the postsynaptic induration is not marked. The postsynaptic elements contain mitochondria with electron-dense matrix and cisternae surroudning the mitochondria. Granular cells show no condensation of clumps of chromatin in the nucleus; there are a small number of ribosomes in the narrow perinuclear space, the cisternae of the laminar complex are not dilated.

In the P group of rats, the ultrastructural changes in some TMF remained similar to degeneration of the "light" or "dark" type on the 2d day of RHG. We failed to detect the state of ultrastructure inherent in hyperexcitation. The rest of the TMF presented an ultrastructure inherent in excitation or, in most cases, indicative of diminished synaptic transmission below the normal level, but more marked than in group C rats on the 2d day of RHG, since there were considerably fewer SV in the TMF axoplasm. As compared to the 30th day of HG, granular cells around such TMF were characterized by reduction of area of chromatin condensation in the nucleus, narrowing of perinuclear space, decrease in number of ribosomes, still dilated Golgi apparatus, which is indicative of decline of cell excitation.

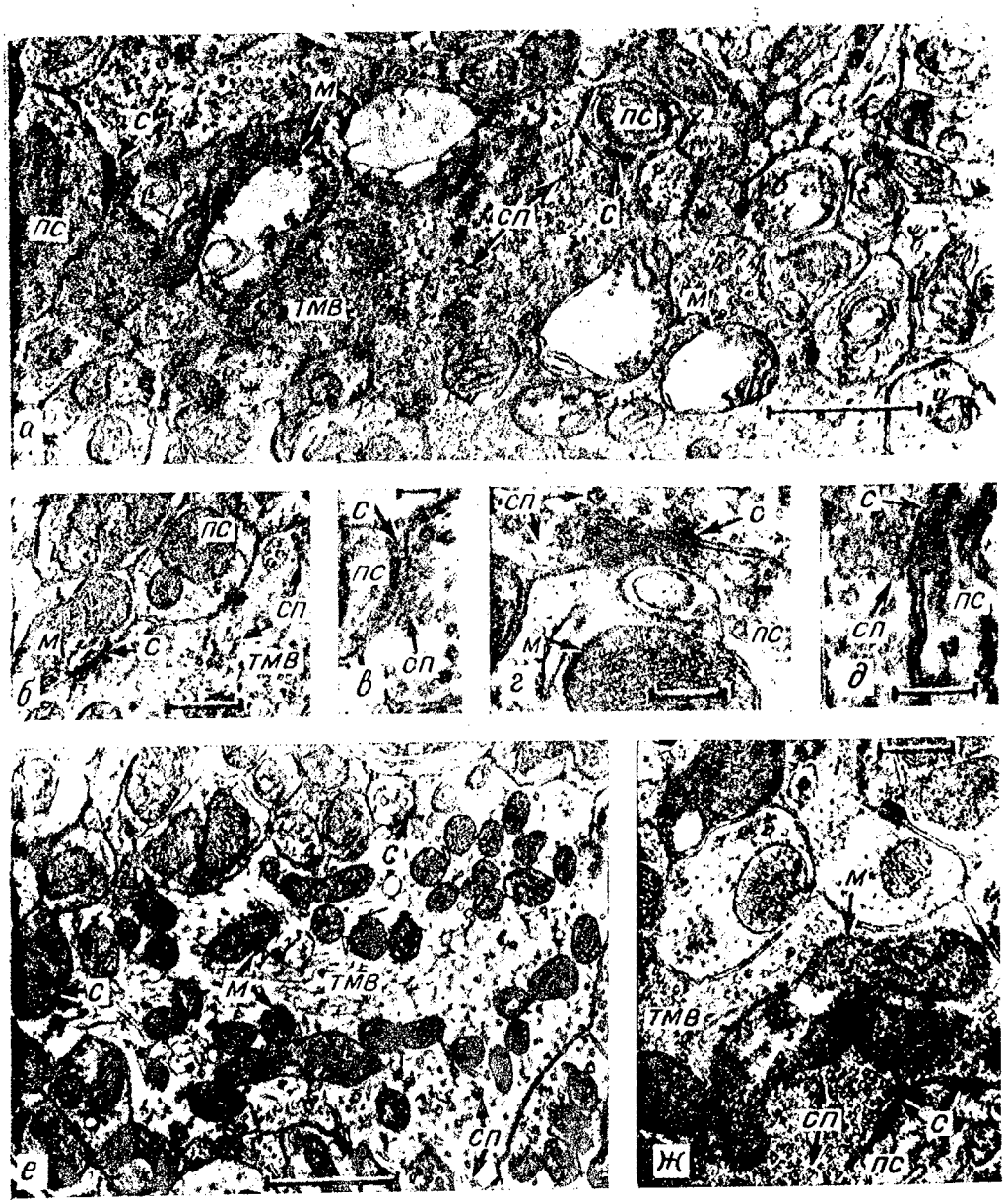

Figure 2. TMF in granular layer of rat cerebellum nodular cortex

а) TMF in state of hyperexcitation; magnification 20,000×; scale 1 μm
б) TMF showing activity in normal physiological range; magnification 25,000×; scale 0.4 μm
в) axodendrite synapse of TMF; activity in normal physiological range; 32,000×; scale 0.2 μm
г) axodendrite synapse of TMF; excitation; 56,000×; scale 0.2 μm
д) axodendrite synapse of TMF; blocked synaptic transmission; 56,000×; scale 0.2 μm
е) TMF of rats submitted to RHG for 2 days; activity below physiological range; 15,000×; scale 1 μm
ж) TMF; hyperexcitation with synaptic transmission block; 25,000×; 0.4 μm
М) mitochondria
С) synapse
ПС) postsynapse

Granular cells situated around "excited" TMF presented the typical ultrastructure of an excited state.

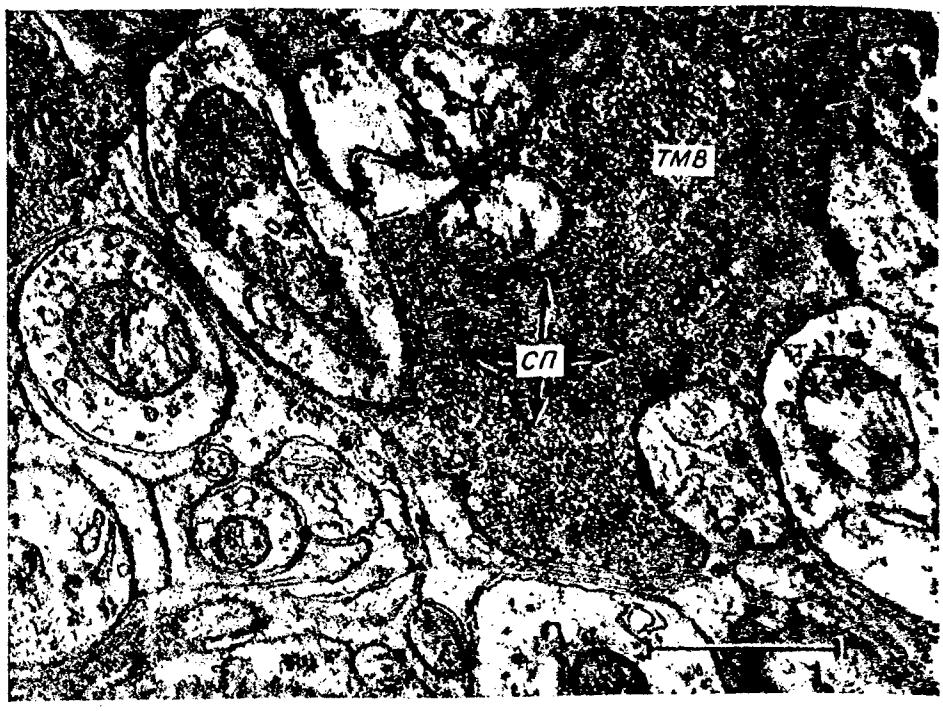

Figure 3. TMF at early stage of changes of the "dark" type; magnification 25,000×; scale 1 μm

ТМВ) terminals of moss fibers СП) synaptic vesicles

The changes remaining in TMF ultracture on the 2d day of RHG, which resembled degeneration of the light or dark type, are attributable to the slowness of their development after exposure to 2.0 G. TMF ultrastructure reflecting a decrease in intensity of synaptic transmission to below the normal level is indicative of inadequacy of earth's gravity to stimulate the otolith system to the level of its normal physiological activity, and it proves that the rat's otolith system was in a state of RHG, since spontaneous activity of gravity-sensitive fibers of the animals' vestibular nerve was diminished for the first 48 h of exposure to weightlessness [10].

On the 7th day of RHG, ultrastructure of group P and C rat TMF did not differ essentially from that of group K rats, which was indicative of the reversibility of changes demonstrated in TMF on the 30th day of HG. Granular cells of group P rats showed some dilatation of laminar complex cisternae, which may be due to their activation on preceding days.

Thus, the changes in RAAS and activity of the utricular receptor cell--vestibular ganglion neuron system occuring on the 2d day of RHG presented the same direction as the changes in these systems in the acute period of adaptation to weightlessness [10, 17], which is indicative of the possibility of using the data

obtained on the 2d day of RHG for analyiss of some effects that occur in mammalian organs and systems in the acute period of adaptation to weightlessness, which are related to perception of change in gravity and adaptation to its new level.

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UDC: 629.78:[612.846:612.866]-06:612.13

EFFECT OF ALTERED CIRCULATION ON HUMAN NYSTAGMIC REACTIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 30 Aug 85) pp 58-62

[Article by V. V. Zaritskiy and Yu. V. Krylov]

[English abstract from source] Optokinetic and vestibulo-optokinetic nystagmus in response to optokinetic and combined vestibulo-optokinetic stimulation applied during head-down tilt was investigated. Tilt-induced circulation changes produced a modifying effect on nystagmic reactions which included a decrease of optokinetic and vestibulo-optokinetic nystagmus and its subsequent recovery after return to the horizontal position. The absolute parameters of vestibulo-optokinetic nystagmus changed depending on the direction of head movements in the sagittal plane relative to the long axis of the body. Some aspects of the relationships between sensory and nystagmic components of vestibular reactions during "conflict" stimulation of the vestibular and visual sensory systems are discussed.

[Text] The problem of space motion sickness (SMS) is drawing the increasing attention of researchers because of its relatively high incidence among the crews of spacecraft [3, 4, 6, 11, 12].

At the present time, most researchers concur with the hypothesis that SMS occurs due to impaired interaction between analyzer systems in weightlessness. Here, unusual optovestibular interactions occupy the main place [7, 12].

The second hypothesis on onset of SMS is change in functional state of the vestibular analyzer as a result of impaired circulation in the basin of labyrinthine vessels when body fluids are redistributed in a cranial direction [3]. Apparently both factors have an effect simultaneously during real flights, and they could induce different effects that are of some relevance to development of SMS, in particular, enhancement of its manifestations.

Our objective here was to investigate the nature of human nystagmic reactions to optokinetic and vestibulo-optokinetic stimulation in the presence of altered circulation with redistribution of body fluids in a cranial direction, which simulates the hemodynamic effects of weightlessness.

Methods

The nature of optokinetic nystagmus (OKN) and vestibulo-optokinetic nystagmus (VOKN) of subjects in antiorthostatic position [head-down tilt] (HDT) was studied using electronystagmography [5]. Vestibular stimulation was produced by rotating the subject while in supine HDT position (-10° angle) on a table about the vertical axis traversing the head, with concurrent graded, forced movement of the head to an angle of ±30° in the sagittal plane. The subject's head was placed on a movable platform connected to the electric drive and control console. To produce optokinetic stimulation (OKS), the head end of the table was equipped with a closed cabin, the ceiling of which consisted of a revolving disk with dark and light bands were alternately arranged, uniformly over the radius.

Fifteen min after moving the subject to HDT, we began to rotate him to the left with the eyes shut until we reached an angular velocity of 120°/s. In this case, the optokinetic disk rotated to the left at the rate of 220°/s. After 3 min of rotation at a constant velocity, the subject opened his eyes and for 10 s we recorded the OKN, after which we began the test using Coriolis accelerations (head movements during rotation) and recorded VOKN. The test was stopped upon appearance of motion sickness symptoms, and the OKN was recorded again.

In a separate series of studies, we checked OKN parameters as a function of target of eye fixation on the optokinetic disk. For this purpose, we made 2 dark bands 3 and 6 cm in width on the disk, which were situated along the circumference at 10 and 30 cm, respectively, from the center.

Health men (44 people) 19 to 42 years of age participated in these studies.

Results and Discussion

Analysis of OKN data listed in Table 1 indicates that there was an increase in amplitude and velocity of the slow phase (VSP) of OKN in the presence of vestibulovegetative manifestations of motion sickness.

Table 1. OKN parameters associated with motion sickness in HDT (-10°)

Conditions	Frequency/s	Overall amplitude, °	Mean amplitude, °	VSP, °/s
I (n = 44)	2,74±0,06	162,54±10,22	6,60±0,21	21,27±0,99
II (n = 43)	2,83±0,07	216,0±9,55	7,45±0,29	25,48±1,37

Note: I and II--before and after rotation, respectively. Here and in Tables 2 and 3, n refers to number of cases.

According to the data in Table 2, the values for VOKN parameters during head movement from the midline up and return to midline were higher than with movements down and back. VSP of VOKN was comparable in absolute values with upward head movements to VSP of OKN, and reliable lower than the latter with downward head movements.

Table 2. VOKN parameters during optic and vestibular stimulation with -10° HDT

Conditions	A			B		
	Number of movements	Overall amplit., °	VSP, °/s	Number of movements	Overall amplit., °	VSP, °/s
I ($n = 44$)	6,80±0,25	56,81±2,94	21,63±0,98	6,06±0,14	49,19±1,55	17,21±0,89
II ($n = 20$)	7,46±0,42	59,80±3,59	23,28±1,50	6,52±0,42	46,89±2,71	17,92±0,98

Key: A) averaged data for one head movement up and back to the midline position
B) for movement down and back
I, II) start and end of stimulation, respectively (during movement)

Table 3. OKN parameters during optic and vestibular stimulation with HDT (-10°; n = 17)

Conditions	Zone 1			Zone 2		
	Number of movem	Overall amplit., °	VSP, °/s	Number of movem.	Overall amplit., °	VSP, °/s
I	32,1±0,5	71,2±1,4	16,0±0,3	30,3±0,3	127,2±2,4	27,0±0,5
II	29,1±0,5	77,0±1,6	14,2±0,2	29,0±0,3	122,1±4,1	26,3±0,7
III	26,3±0,6	63,5±2,1	13,6±0,2	43,3±0,2	137,6±3,5	31,0±0,6
IV	26,1±0,3	72,6±1,9	14,9±0,4	30,1±0,2	161,4±4,4	34,8±0,8
V	30,3±0,2	85,4±2,3	18,5±0,3	32,3±0,3	145,3±3,7	32,0±0,7
VI	31,5±0,4	73,3±1,8	16,0±0,3	28,1±0,4	132,2±3,0	28,4±0,5

Key: I) horizontal position, $\omega = 0°/s$
II) HDT, $\omega = 0°/s$
III) HDT, $\omega = 120°/s$
IV) HDT, $\omega = 120°/s$
V) HDT, $\omega = 0°/s$
VI) horizontal position, $\omega = 0°/s$ (ω is velocity of tilt table)
I-III) before movement
IV-VI) after movement

OKN parameters diminished when subjects were changed to HDT, particularly when tracking optokinetic stimuly closer to the center of the disk (Table 3). Rotation led to further decrease in number of OKN movements when gazing closer to the center (zone 1), while amplitude and VSP showed virtually no change. When tracking stimuli further from the center of the disk (zone 2), the values of all these OKN parameters increased.

Thus, with combined optic and vestibular stimulation in HDT, we demonstrated differences in the various characteristics of the nystagmic reaction to head movements upward and downward in relation to the middle axis of the body. With upward head movement, the vestibular and optic components of VOKN were in the same direction, and the absolute values of VOKN were higher than with downward head movements, when both components of VOKN presented the opposite direction. The inhibitory effect of the vestibular component on VOKN was more marked. This

is perhaps related to the fact that downward movement (posterior Coriolis) is a stronger vestibular stimulus [6]. Most of the subjects reported that they felt worse with downward head movements.

The data on the possibility of enhancing and inhibitory effect of the optic component on VOKN are consistent with the results of studying VOKN using tests with cumulative Coriolis accelerations in an optokinetic drum [1, 13].

In our studies, we found a tendency toward some increase in existing difference between VOKN parameters with upward and downward head movements during development of motion sickness. The increase in this difference occurred mainly due to increment of VOKN at the phase of upward movement, i.e., when the vestibular and optokinetic components of the oculomotor reaction presented the same direction.

Analysis of VOKN parameters and their correlation with sensory perceptions (illusion of rocking that occurs when the head is moved during rotation) revealed that the subject developed the sensation of faster rotation when his eyes were shut during upward head movement and that of slower rotation, to the extent of a complete stop, with downward movement. Occasionally there was the sensation of movement in the opposite direction. Then the vestibular nystagmus showed a change in direction, concurrently with change in direction of illusory sensations, i.e., with the eyes shut, the vestibulosensory and vestibulosomatic components correspond to one another in the test with use of Coriolis accelerations. With OKS in the direction of movement of the tilt table, most subjects developed the sensation of movement in the opposite direction, which coincided with the direction of VOKN. This instance of inconsistency between oculomotor reaction and sensory sensations can probably be interpreted as a conflict between the sensory and comatic components of the vestibular reaction. Perhpas this is the factor that worsens tolerance to the test with combined optic and vestibular stimuli in the mode used and, consequently, it worsens the subject's wellbeing when he moves his head downward, when the direction of perception of motion did not coincide with the direction of OKN. With upward head movement, the sensory and nystagmic components of the vestibular reaction, as well as direction of OKN, coincided with the direction of movement, and the subjects reported some improvement of their feelings.

The demonstrated disagreement between the nature of changes in frequency, amplitude and VSP of OKN when tracking visual stimuli at a distance of 10 and 30 cm from the center of the optokinetic disk, which correspond to different linear velocities of optic stimulation and, accordingly, different strain of oculomotor muscles, confirms the validity of the opinion held by researchers, that there are intermediate neuronal elements between the vestibular and oculomotor nuclei that participate in generation of nystagmus [8, 9].

In the same series of studies, we made the rather important finding that there was modification of OKN with redistribution of body fluids in a cranial direction. Apparently, impairment of hemodynamic stability in the region of the peripheral and central parts of the vestibular analyzer led to a change in its functional state.

Thus, our findings confirm the data known in clinical labyrinthology [2, 10] about the high sensitivity of the vestibular analyzer to hemodynamic changes, and they indicate indirectly that, at the early stage of adaptation to weightlessness during spaceflights, the hemodynamic factor perhaps alters the functional state of the vestibular analyzer and, along with other factors, may be an element in the etiopathogenesis of space motion sickness.

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THRESHOLDS OF LONG-LATENCY-PERIOD POTENTIALS AND SENSATION OF MOTION EVOKED IN MAN BY LINEAR ACCELERATIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 14 Mar 86) pp 62-66

[Article by K. F. Trinus]

[English abstract from source] Forty-seven healthy test subjects were exposed several times each to linear acceleration of varying value. Depending on the acceleration value, they reported subjectively three types of sensations at the threshold level: nondiscriminated in terms of direction (P_1, $\bar{a}$ = 8.0±2.5 cm/sec^2), inverted (P_2, $\bar{a}$ = 12.4±2.5 cm/sec^2) and discriminated (P_3, $\bar{a}$ = 16.1±3.5 cm/sec^2). The acceleration value at which P_2 was recorded caused most typical responses in different test subjects whereas that at which P_3 was recorded induced greatest individual variations. Evoked potentials in response to linear acceleration were recorded in such a manner which excluded potential instrumental artefacts or possible contribution of eye movements, excitation of the hearing organ and muscle tone changes. The data obtained indicate that acceleration-induced evoked potentials are predominantly of vestibular origin and consist of three peaks, viz P_1, N_1 and P_2, the latencies of which are equal to 31.3±7.2, 69.1±9.1 and 157.6±10.5 msec at the threshold where they emerge. The peak P_1 is most variable, the peak N_1 is most stable and the peak P_2 is characterized by the largest ratio of the interindividual variation to the individual variation.

[Text] At the present time, the method of evoked potentials (EP) is used to determine the state of analyzers; it permits evaluation of the nature of processing of sensory information by concrente brain structures [9, 7]. At the same time, there have been only a few attekpts to record vestibular EP (VEP) on animals [4] and long-latency EP due to the effect of accelerations (A-EP) on man [6].

Methods

A 2Ts1102 chair, the lifitng pedal of which was replaced with a lever about 1.5 m in length, served as the source of linear accelerations (Figure 1). By shifting 2- and 5-kg weights along this lever, linear accelerations upward were set in

the range of 0-50 cm/s. The lever was raised manually and held in place by a catch. When the catch opened, weight *1* dropped under the effect of gravity and lowered lever *2*. The pressure was transmitted from the lever through piston *3* to cylinder *4*, as a result of which oil from cylinder *4* was pumped via connective tube *5* into cylinder *6*, and this led to 12 cm elevation in 300-400 ms of the moving part *7* of the chair. There was a button in the arm of the chair, which the subject depressed upon appearance of moving sensation. Plate contact *8* was actuated when the chair began to rise, and this started the SM-1 computer, into which were inputted the signals from the acceleration recorder and EEG. Accelerations were measured with an SP23a potentiometer, the housing *9* of which was attached to the chair stand, while the cursor *10* was attached to its movable part. The immediate tension readings taken from the potentiometer, which are proportionate to the degree of chair elevation, were fed to the computer. From the second derivative of change in tension as a function of time, determination was made of accelerations. After each elevation, the chair was smoothly returned to its initial position.

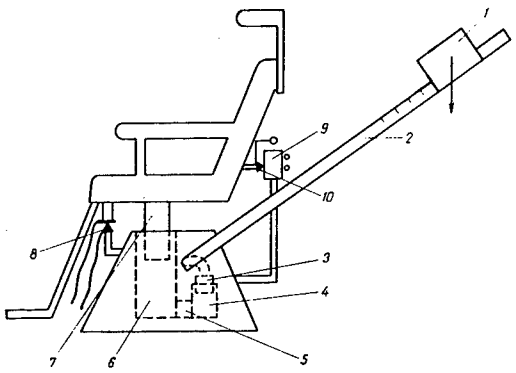

Figure 1.
Drawing of source of linear accelerations. Explained in the text.

The light was turned off in the room, the subject was seated in the chair and asked to relax. The chair was raised several times at different speeds until the subject reported sensation of movement. Then, we began to record A-EP in the region of demonstrated accelerations. For this purpose, we placed three metal electrodes on the subject's head: active one (vertex), silent one (mastoid process) and ground (forehead). To rule out the influence of extraneous noises, plugs were inserted in the subject's ears and he wore ear muffs, which provided noise suppression of about 40 dB.

EEG signals were fed through amplifier UBF4-03 with 2.5-15 Hz bandwidth to the input of the computer. Synchronously with elevation of the chair, a segment of the EEG lasting 256 ms was fed into the computer approximately every 15 s. After 12 accumulations, the resultant block of A-EP consisting of 256 points was recorded on a magnetic carrier and projected in analogue form on the display screen. Upon detection of an artefact, the next EEG run was not used in storage. An EEG signal which exceeded the given size of the bit arrangement of the analog-to-digital converter was considered an artefact.

In all, we conducted 84 tests on 47 subjects, 22 of whom were tested 3-4 times at 10-20-day intervals. The subjects included 36 healthy individuals of both sexes 14 to 38 years of age and 11 patients, 2 of whom suffered from bilateral labyrinthine areflexia, 4 had Meniere's disease and 5 had neuritis of the acoustic nerve associated with vestibulopathy.

We conducted 5 series of studies: in the 1st series determination was made of subjective sensations of motion induced by linear accelerations in healthy subjects (53 tests on 25 subjects, in the course of which 131 records were made); in the

2d series, we determined A-EP of healthy subjects (64 tests on 22 individuals, in the course of which 137 A-EP were recorded); the 3d series was a control to assess the contribution of possible artefacts and different sensory and motor systems to the A-EP), the 4th and 5th series involved determination of subjective sensations and A-EP, respectively, of patients.

Results and Discussion

In response to threshold linear accelerations, healthy subjects developed all three types of sensations: at first it was the sensation of motion that was not discriminated as to direction; with increase in acceleration, all of them indicated the opposite from actual direction of movement and, finally, they correctly indicated its direction. Further acceleration led to appearance of a sensation of a jolt perceived by muscles of the back and legs. The magnitude of accelerations with which the above-described sensations were recorded were arbitrarily designated as the thresholds of nondiscriminated, inverted and discriminated sensations, and they were expressed as P_1, P_2 and P_3, respectively. For P_1, acceleration constituted 8.0±2.5 cm/s^2, n = 26, N = 49 (n is number of subjects and N is number of tests); for P_2, the figures were 12.4±2.5 cm/s^2, n = 24, and N = 48; for P_3, 16.1±3.5 cm/s^2, n = 23 and N = 37. The coefficients of variation of threshold accelerations constituted 31.2, 23.2 and 21.7%, respectively.

We tested 12 subjects either several times on the same day or at intervals of a few days. We determined individual and interindividual coefficients of variation of threshold accelerations, and they were calculated separately for tracings obtained on the same day. P_1 threshold accelerations were notable for the greatest variability, and the interindividual coefficients of variation recorded both on the same day and on different days were virtually the same (24.1 and 25%). Individual coefficients recorded in both instances were also close (16.1 and 19.1%). At the same time, there was a difference between individual and interindividual coefficients. This indicated that each individual has his own range of threshold accelerations at which nondiscriminated sensations are evoked. P_2 threshold accelerations were the most stable in different subjects. This is also indicated by the fact that the interindividual and individual coefficients of variations recorded both on the same day (10.3 and 12.8%) and on different days (11.6 and 14.0%) were virtually the same. P_3 threshold accelerations were found to be the most variable, and this referred to appearance of discriminated direction of sensation of movement; this group also presented significant prevalence of interindividual coefficients of variation over individual ones (33.6 and 22.4% for coefficients of variation on the same day, 16.3 and 8.7%, on different days).

In order to determine whether the thresholds of sensitivity are a function of psychological distinctions, 14 healthy subjects out of 27 were tested by the methods of binary probabilist training (Footnote)(The tests were performed by Ye. V. Skalko) [1]. The subjects were presented with 5 series of 40 cues each in random order. Appearance of a light served as a positive cue and a pause, as a negative one. We asked that the subjects predict appearance of a positive or negative signal. On the basis of processing of the results, we determined whether a given subject had a tendency toward overestimation (1st group) or underestimation (2d group) of the probable threshold event. Prior comparison of the results to P_1 acceleration levels revealed that the 1st group developed the

above sensations at accelerations of 6.2±1.8 cm/s^2 (n = 4) and the 2d group, 11.5±1.7 cm/s^2 (n = 2). There was also an intermediate group of subjects, which was the largest (n = 8). These data indicate that the thresholds of perception of linear accelerations probably depend on individual psychological distinctions.

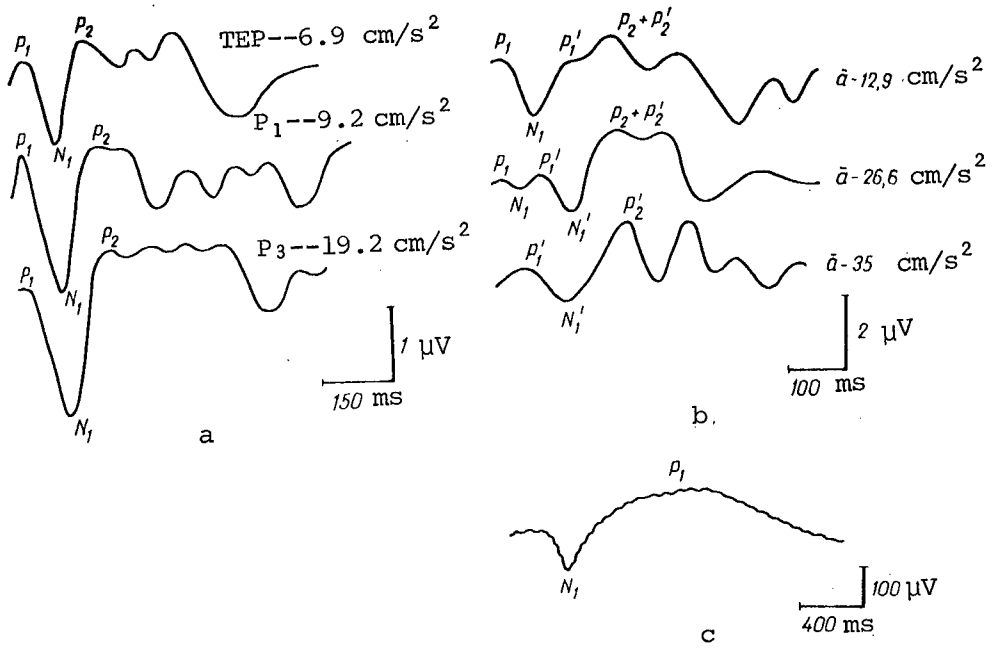

Figure 2. Examples of A-EP in healthy subjects

a) accelerations within the range of threshold subjective sensations
b) accelerations exceeding threshold subjective sensations
c) vestibuloocular response to accelerations

The typical A-EP curve (Figure 2a) consisted of three most stable peaks: two positive ones in relation to the vertex (P_1 and P_2) and one negative one (N_1). The Table lists the mean latency periods of the main peaks obtained with different accelerations. It should be noted, first of all, that the data scaled to subjective sensations virtually coincide with those given as numerical values of accelerations. In both instances there is a tendency toward shortening of latency peaks with increase in accelerations. Shortening of latency periods of the peaks for acoustic and somatic EP with increase in stimulus has been described in the literature [4, 10], and it is apparently a universal property of EP of all modalities. It was also found that, in all cases, A-EP was recorded with accelerations below the threshold of perception of movement. The A-EP (TEP) threshold was arbitrarily selected for acceleration of 5.7±1.8 cm/s^2 (n = 6, N = 13), at which the signal:noise ratio was at least 2:1. It is rather important that the latency period of P_2 decreases the most as we go from TEP to P_1. The most substantial shortening of peak latency periods occurs with change from P_1 to P_2 for numerical values of accelerations from less than 5 cm/s^2 to those in the range of 5 to 10 cm/s^2; with change from P_2 to P_3, there is appreciable change only in latency period of N_1 peak.

Latency periods of peak A-EP and their coefficients of variation at different levels of acceleration

	P_1						N_1						P_2					
	$M \pm m$	K	K_{1m}	K_{1i}	K_{2m}	K_{2i}	$M \pm m$	K	K_{1m}	K_{1i}	K_{2m}	K_{2i}	$M \pm m$	K	K_{1m}	K_{1i}	K_{2m}	K_{2i}
TEP	31,3±7,2	23,2	13,0	1,4	—	—	69,1±9,1	13,2	15,6	5,1	—	—	157,6±10,5	6,7	3,3	0,9	—	—
≤5	34,1±8,8	25,8	—	—	16,4	13,7	72,6±8,4	11,6	—	—	5,8	7,3	145,9±16,7	11,4	—	—	7,0	7,0
P_1	30,0±8,5	28,3	21,4	17,2	30,6	17,3	70,3±12,4	17,8	14,3	10,4	11,9	10,1	145,5±18,4	12,6	10,6	6,7	11,9	6,4
5–10	27,0±7,0	25,9	17,5	11,8	19,4	11,8	68,3±8,6	12,6	9,7	7,3	9,5	8,0	149,9±16,0	10,7	13,6	6,8	8,5	5,7
P_2	23,0±6,4	27,8	27,9	14,8	28,9	13,3	64,2±6,8	10,6	9,1	8,9	8,7	6,6	133,9±16,0	11,9	9,7	8,0	9,5	6,2
10–15	26,6±8,8	33,1	21,6	22,7	21,3	20,5	64,9±8,9	11,4	11,4	10,2	12,4	7,5	132,1±18,9	14,2	9,5	10,1	11,1	9,9
P_3	22,4±6,4	28,6	16,3	21,8	11,4	17,1	57,0±7,4	13,0	8,3	8,7	12,7	5,0	136,9±22,4	16,2	10,9	9,7	12,0	7,1
>15	19,8±6,1	30,8	18,3	21,1	21,3	12,2	55,0±6,9	12,5	5,3	7,8	8,7	6,4	143,2±15,6	10,9	6,7	11,0	7,0	8,4

Key: K) coefficient of variation of latency periods, overall
K_{1m}) interindividual coefficient, on different days
K_{1i}) individual coefficient, on different days
K_{2m}) interindividual, on the same day
K_{2i}) individual, on the same day

A more thorough examination of coefficients of variation revealed that the widest variability of latency period is noted for the P_1 peak and the lowest, for N_1. Variability of P_2 peak latency period increases progressively in the transition from TEP to P_3, and the greatest jump, from 6.7 to 12.6%, is noted between TEP and P_1. The latency period of P_2 is subject the most to individual differences, whereas latency period of N_1 is the most stable.

With increase in accelerations, all of the healthy subjects reported appearance of the sensation of a jolt to leg and back muscles, and the recorded potential became very complex (Figure 2b). We could distinguish in it peaks referable to the ones we described (P_1, N_1 and P_2), on the one hand, and to somatosensory EP (peaks P_1'', N_1'' and P_2''), on the other hand. Upon further increase in accelerations, we recorded only somatosensory EP analogous to the one described in the literature [2]. The same EP was recorded on 2 patients with bilateral labyrinthine areflexia at accelerations of about 25 cm/s^2, as well as in tests where the trunk was exposed to accelerations while the head was immobilized. In this case, accelerations exceeded 20 cm/s^2 (n = 6).

We used a model of a subject, in the form of a mannekin secured in the chair, to assess the effect of electromotive forces that arise upon displacement of conductors connecting the electrodes to the amplifier input. We failed to record a signal resembling A-EP.

To assess the possible contribution to A-EP of oculomotor potentials, we examined the oculogram (taken on 6 healthy subjects) recorded with elevation of the chair (Figure 2c). The latency period of the first peak on the oculogram was about 400 ms, i.e., it was considerably longer than the last peak of A-EP.

Testing of acoustic EP and A-EP in the same subjects revealed that the latency period peaks of A-EP were 10-30 ms shorter than for acoustic ones. Delivery of white noise of 100-110 dB did not affect A-EP.

With rigid immobilization of the head and trunk to the movable part of the chair, we failed to demonstrate differences, as compared to control signals. When we

summed up the myogram tracings for cervical muscles during elevations, we also failed to record a signal similar to A-EP.

The results of control studies warrant the assumption that the A-EP that we recorded are determined primarily by stimulation of vestibular receptors.

It should be noted that authors who previously recorded VEP did not conduct control tests to rule out artefacts. The vestibuloocular reaction was taken for the sought VEP in [8]. To record VEP, it is important for there to be good synchronization and properly matched slope of acceleration build-up, since otherwise there is considerable extension of latency periods of peaks and an increase in number of accumulations needed. This is probably why some authors found peak latency periods in the range of 200-500 ms [10]. Special attention should be given to having clean surfaces and proper lubrication of friction parts in the moving device, since the slightest flaws could lead to dominance of the somatosensory analyzer, and subjects will perceive vibration and jolts. The fact that some researchers recorded a somatosensory potential that they could not separate from the vestibular one may be attributed to this, as well as to significant accelerations [1].

We determined the diagnostic value of the above findings in a study of sick people. According to preliminary data, individuals with unilateral hyporeflexia (Meniere's disease; $n = 4$), the subjective thresholds of sensitivity were close to normal (probably due to an intact labyrinth), but peak latency periods on the contralateral side, in relation to the lesion, were increased. A particular increase was observed in the range of accelerations corresponding to P_1. In individuals with bilateral hyporeflexia or vestibulopathy ($n = 5$), there was extension of latency periods of A-EP peaks and elevation of subjective thresholds of sensitivity.

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MATHEMATICAL MODEL OF THE OTOLITH

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 8 Aug 85) pp 66-70

[Article by A. V. Kondrachuk, I. Ye. Shchechkin and S. P. Sirenko]

[English abstract from source] This paper describes a mathematical model of the otolith of mammals represented as a system with parameters of distribution. Two versions of the model are analyzed and the lowest frequencies of natural oscillations of the system are evaluated.

[Text] Motion sickness, which occurs when man works in modern transportation vehicles, including aircraft and spacecraft, is related primarily to functional distinctions of the vestibular system in moving systems. The vestibular system consists of two receptor elements which interact with one another but perform different functions: semicircular canals, which record angular accelerations, and otoliths, which record linear accelerations and orientation of the head in relation to the direction of gravity, actually the gravity receptor [1, 3].

It is assumed that motion sickness that occurs during spaceflights is largely related to change in otolith function in weightlessness [9].

The otolith is formed by an otolith membrane (OM) and receptor epithelium--the macula--situated under it. The OM is flexibly attached to the macula and is made up of otoconia (calcite crystals) submerged in a gelatinous substance [1, 12]. The OM has a density that is about 2.5 times greater than that of the surrounding endolymph. The right and left otoliths consist of three otoliths each, and they are situated approximately in mutually perpendicular planes.

It is believed that stimulation of otolith receptors occurs when the OM shifts parallel to the macula under the effect of a force (inertia or gravity) and, interacting with receptor cell hairs, bends them [1].

In otolith models that exist at the present time, the OM was considered to be an absolute solid that moves in the plane of the macula [2, 5, 10, 15]. To describe OM dynamics, the equation for a damped one-dimensional oscillator was proposed [15], and estimates were made of its parameters of elasticity and viscous friction in experiments on rigid otoliths of fish. In subsequent works, efforts were concentrated mainly on obtaining theoretical estimates of the effect of endolymph on behavior of this model [2, 5].

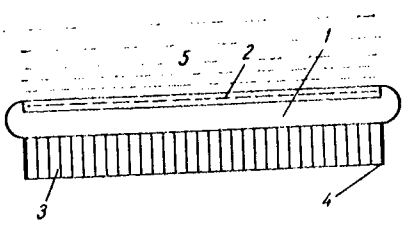

Figure 1.
Drawing of otolith structure
1) OM
2) otoconia layer
3) trabeculae
4) marginal supports
5) endolymph

Yet, as shown by experiments [6, 11], the mammalian OM is a deformable solid with degrees of freedom related to deformation. Tnis means that movement of the OM does not merely amount to movement of a tangible point, but resembles that of an elastic plate with fixed edges, or a flexible membrane, or even a drop of viscous fluid [6], i.e., the OM is a system with distributed parameters. It can be assumed that resonance effects in degrees of freedome of OM due to deformation may be responsible for functional impairment of the otolith in moving vehicles, including spacecraft.

On the basis of the results of studying the structure of otoliths [11, 12], let us assume that the OM is a round, heavy, elastic plate resting on a resilient base formed by a system of supporting trabeculae [rods] (Figure 1). To assess the behavior of this OM model, let us examine the free transverse oscillations of such a plate, which are described by the following equation [8]:

$$\Delta^2\zeta + \frac{m}{D}\frac{\partial^2}{\partial t^2}\zeta + \frac{c}{D}\zeta = 0 \qquad (1)$$

where $\Delta = \frac{\partial^2}{\partial r^2} + \frac{1}{r}\frac{\partial}{\partial r}$, $\xi = \xi(r, t)$ is a function of deflections; $D = \frac{Eh^3}{12(1-\sigma^2)}$

is cylindrical strength, E is modulus of elongation [Young's modulus], h is plate thickness, δ is Poisson's ratio, c is specific coefficient of base lasticity and m is mass of plate area unit.

Assuming that $\xi(r, t) = \xi(r)e^{-i\omega t}$ and with consideration of (1) we shall have:

$$\Delta^2\zeta - k^4\zeta = 0, \qquad (2)$$

where $k = \frac{\omega^2 m - c}{D}$, from which we have:

$$\omega^2 = \frac{k^4 D + c}{m}. \qquad (3)$$

With $r = 0$, the solution of equation (2) has the following appearance:

$$\zeta(r) = A_1 J_0(kr) + A_2 I_0(kr), \qquad (4)$$

where $I_0(kr)$ is Bessel's function, $I_0(kr) = J_0(ikr)$ while coefficients A_1 and A_2 are calculated from the boundary conditions, with $r = a$ (a is plate radius).

Let us examine two types of boundary conditions that correspond approximately to existing descriptions of marginal attachment of OM [12].

A. Let the marginal support trabeculae consist of a uniformly distributed set of nonelastic rods which bend when the edges of the plate bend, developing a moment of force. Then, with $r = a$, we can write down:

$$\zeta = 0, \quad \frac{\partial^2}{\partial r^2}\zeta + \frac{\sigma}{r}\frac{\partial}{\partial r}\zeta = -\frac{G}{a}\frac{\partial}{\partial r}\zeta, \tag{5}$$

$$\text{where } G = \frac{4E_K I_K n a}{dD};$$

E_K is Young's modulus of marginal attachment, $I_K = \frac{\pi R^4}{4}$ is moment of inertia, n is density of rods per unit outline length, d is rod length and δ_K is Poisson's ratio for marginal attachment.

Using (4) and (5), and solving the corresponding special equation in relation to $\Psi = ka$, it is not difficult to find the lowest value, Ψ_H, which lies between 2.25 and 3.05, depending on values of G and σ.

B. In the case of resilient attachment of OM on the margin, for $r = a$, we can write down:

$$\frac{\partial^3}{\partial r^3}\zeta + \frac{1}{r}\frac{\partial^2}{\partial r^2}\zeta - \frac{1}{r^2}\frac{\partial \zeta}{\partial r} = -\frac{K_y}{D}\zeta,$$

$$\frac{\partial^2}{\partial r^2}\zeta + \frac{\sigma}{r}\frac{\partial}{\partial r}\zeta = 0, \tag{6}$$

where Ky is coefficient of elasticity of attachment.

From (6) and (4), we find that the lowest value for Ψ_H is between 1.05 and 2.45, depending on the values for Ky and D.

According to (3), elasticity of base c and rigidity of OM D are included additively in frequency, and this is attributable to the selected model for the base. For this reason, let us first estimate c. Since the resilient base in this model is approximated by a system of resilient trabeculae (rods), it is first necessary to determine the elasticity of one such rod. According to structural data [1, 12], supporting trabeculae can be compared to nondeformed, bent rods that are rigidly attached with one end to the macula and the other, to the OM. The coefficient of elasticity of such a rod is estimated using the formula:

$$c_1 \sim \frac{\pi^2 I_1 E_1}{R^3_4} \quad [4],$$

where R_4 is the radius of rod flexure ($R_f >> d$). Considering the radius of the rod to be $R_1 \sim 10^{-4}$ cm, we have $c_1 \simeq 2 \times 10^{-8} E_1$. Hence, $c = c_1/S_0 \sim 10^{-6} E_1$, where S_0 is OM area.

Using the same values for parameters and the obtained numerical values for Ψ_H, it is not difficult to obtain:

$$Dk^4 \sim 10^{-2}E.$$

Considering that $E \simeq 10^4 - 10^5$ dyne/cm [14], we have $Dk^4 >> c$, consequently, lowest frequencies $f = \omega/2\pi$ of such a system are determined by the properties of OM itself. For this range of parameters, they are in the ranges of 0.66-6.6 Hz in case A and 0.14-1.4 Hz in case B.

For the selected model of a resilient base, let us determine strength of the system with a shift of OM along the macula, using the formula:

$$c_V = \frac{3k_z E R_1^2}{d^2 2},$$

where k_z is the ratio of area occupied by rod bases on OM to OM area. Inserting values of parameters in this formula, we shall have $c_k \simeq 5 \cdot 10^4 k_z - 5 \cdot 10^5 k_z$. With k_z 0.1-0.01, we shall have ck 10^2-10_4 dyne/cm. The experimentally found value for c_v is 10^3 dyne/cm [15].

Since OM is in the endolymph, when estimating the transverse oscillations of OM we must take into consideration the movement of attached fluid (ж), which leads to decrease in frequency of OM oscillation. Knowing density of OM and endolymph, it is not difficult to calculate the lower frequency of transverse oscillations of OM [7]:

$$\text{OM [7]: } f_A^{ж} = \frac{f_A}{\sqrt{1+\beta}} \simeq 0{,}16-1{,}6 \text{ Hz};$$

$$f_B^{ж} = \frac{f_B}{\sqrt{1+\beta}} \sim 3{,}4 \times 10^{-2}-0{,}34 \text{ Hz},$$

where $\beta = 0{,}6689 \frac{\gamma_1 a}{\gamma h}$, γ_1

is density of endolymph and γ is density of OM. Nonuniformity of distribution of otoconial mass--noncoincidence of center of mass of otoconia with that of OM--also leads to a decline of intrinsic OM frequencies. Let us mention that the frequencies of most probable sinusoidal motion are in the range of 0.1-0.3 Hz [13].

These estimates indicate that OM parameters allow for existence of intrinsic transverse oscillations of OM at a low frequency, and thus there may be resonance effects with exposure to exogenous forces containing a low-frequency component (pitching of a ship). Consideration of viscous friction does not lead to a change in values for intrinsic OM frequencies, but determines the nature of damping of resonance waves. Since primarily a displacement of the OM parallel to the macula is an adequate stimulus for otolith receptors, occurrence of OM motion associated with deformation, in particular, transverse oscillations with which the flexure of hair cells is directed alternately toward movement

of the center of mass and way from it leads to unusual stimulation of the aggre gate of otolith receptors, and it could be one of the causes of motion sickness

Let us discuss two experimental facts in which, in our opinion, there is manifestation of the distinctive dynamics of OM as a system with distributed parameters.

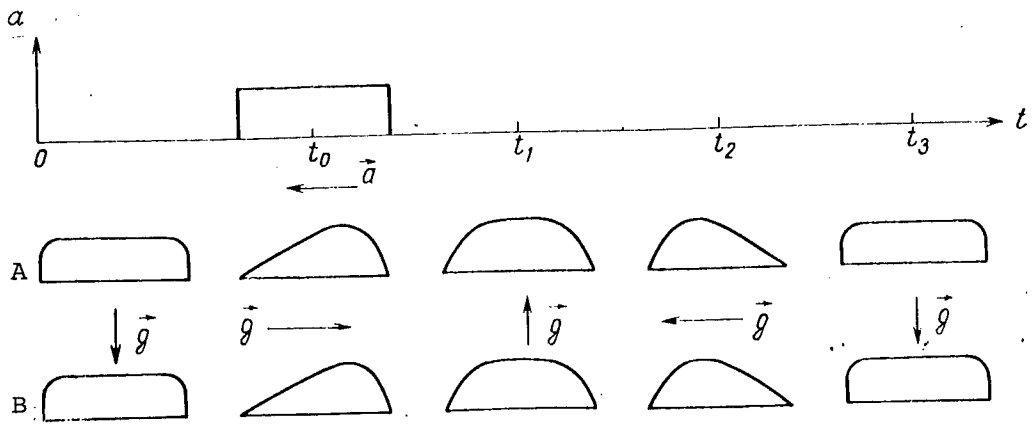

Figure 2. Qualitative behavior of OM as a system with distributed parameters

A) brief linear acceleration a parallel to macula (top--linear acceleration as a function of time for the corresponding OM states)
B) rotation of OM in relation to vector of acceleration of earth's attraction $\vec{g}$ (somersault)

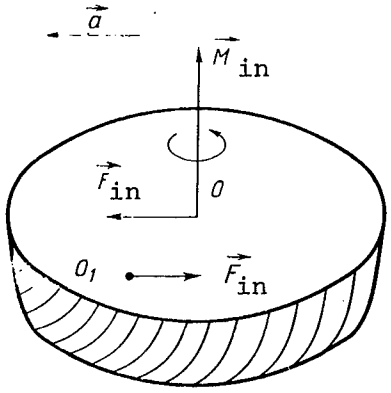

Figure 3.
Possibility of OM twisting when the center of "rotation" and center of mass do not coincide under the effect of linear acceleration

$\vec{a}$) acceleration
$\vec{F}_{in}$) inertial force
$\vec{M}_{in}$) moment of inertial force
0_1) center of mass
0) center of "rotation"

Figure 2A illustrates the behavior of th described mathematical model of OM under the effect of linear acceleration parall to the macula (Figure 2A). Figure 2B shows behavior of OM in the case that corresponds to a 360° turn (somersault). A comparison of Figure 2 A and B shows that different types of movement (linear and angular accelerations) can lead to similar dynamic states of OM if the possibility of its deformation is taken into consideration, and consequently to similar physiological reactions.

As it was shown in [10], with rotation of the vector of acceleration, the occu ring nystagmic reaction may be due to "twisting" of OM. It is not difficult show that, within the limits of the mod proposed in [10], such otolith behavior impossible. However, if we assume that the center of OM mass and center of

"rotation" do not coincide, there can be a moment of forces that strives to turn the OM. It must be noted that, in this case, "twisting" of OM is also possible under the effect of linear acceleration (Figure 3).

Thus, the conception of mammalian OM as a system with distributed parameters broadens appreciably the range of possible dynamic behavior of otoliths.

We wish to thank A. A. Shipov for discussing the issues covered in this article.

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REACTIVITY OF ADRENOSYMPATHETIC SYSTEM AND TOLERANCE TO EXERCISE LOAD DURING REPEATED EXPOSURE TO STATIONARY MAGNETIC FIELD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 4 Sep 85) pp 70-73

[Article by L. D. Klimovskaya and L. V. Kokoreva]

[English abstract from source] For 30 days rats were exposed daily 3 h a day to a constant magnetic field of 1.6 T. The time within which the rats were swimming with a load until they were fatigued was measured and the concentration of catecholamines in blood and adrenals was determined. Two stages of the response to the magnetic field were identified. During the first stage (1-15 days) physical work capacity increased and the reactivity and reserve ability of the sympatho-adrenal system (SAS) grew. During the second stage (30th day and early recovery period) work capacity returned to normal and the SAS reactivity decreased, although the catecholamines stored in the adrenals remained unchanged. These findings indicate that the SAS is involved in mechanisms underlying changes in work capacity and adaptation processes during exposure to a constant magnetic field.

[Text] The sympatho-adrenal system (SAS) is actively involved in forming the body's reaction to physical loads [2, 4]. Exposure of rabbits, mice and rats to stationary magnetic fields (SMF) of high intensity elicits an increase in concentration of blood catecholamines (CA) [5-7]. There is no information in the literature concerning the nature of SAS reactions to physical loads in animals exposed to SMF, although they are relevant to comprehension of the genesis of changes in physical work capacity under such conditions. The long-term effects of strong SMF are of some interest, since they permit evaluation of functional integrity of the SAS and its capacity to react adequately to extreme environmental factors.

Our objective here was to test the effect of a physical load on blood and adrenal CA content in rats, and to assess their physical work capacity during long-term interrupted exposure to high-intensity SMF.

Methods

This study was conducted on 170 male albino rats. The magnetic field was generated using an SP-57A electromagnetic with pole tips in the form of a circle with a 450-mm radius and 100-mm air space between them. Magnetic induction of the field in a 380-mm radius remained virtually unchanged, decreased by 20% toward the edge of the polar tips. The magnetic field was strictly stationary. Rats were exposed to total-body vertical SMF with induction of 1.6 T for 3 h a day for 30 days. Control animals were kept in the same room under analogous conditions in a phantom of polar tips made of duralumin. They were tested immediately after exposure to SMF, then on the 1st, 5th, 15th and 30th experimental days, as well as 1 day after the last exposure, including experimental and control animals simultaneously. The swimming test was used as a physical load. Each rat swam separately and once with a weight equalling 10% of its body weight; water temperature was 32°C. To assess physical work capacity, we recorded swimming time until they were totally tired; the rats were decapitated. Epinephrine (E) and norepinephrine (NE) levels in the adrenals and blood plasma were measured by fluorimetry.

Results and Discussion

It was shown previously [7] and confirmed here that blood E content is increased in the course of exposure to SMF with induction of 1.6 T for 1 month at the rate of 3 h per day, and this was particularly marked in the rats during the first 2 weeks (200-300% as compared to control level). After exposure 30 times, blood E level constituted 140%, while complete normalization occurred within 1 week after discontinuing exposure to the SMF. In intact rats who swam to the point of total fatigue, there was reliable increase in blood E content (9.21 ± 0.77, versus 5.82 ± 0.43 in the control). The effect of SMF on this response depended on the frequency of exposure. In rats who swam after 1-15-fold exposure to SMF there was virtual summation of effects of the magnetic field and exercise, and the concentration of E in blood reached higher levels than with separate exposure to each of these factors (Figure 1). Blood E level was lower in rats that swam after 30-fold exposure to SMF than under the effect of the magnetic field or exercise alone. Thus, the physical load at the start of intermittent exposure to SMF with a high blood E level causes its further elevation, whereas at the end of the experiment, in the presence of a lower concentration of the hormone, it leads to even greater decline.

Evaluation of adrenal CA content is important to interpretation of the demonstrated changes. As it was shown previously [7], levels of E and NE in the adrenals remained at the control level or somewhat above it throughout the month of exposure to divided doses of SMF with induction of 1.6 T. Analogous results were obtained when SMF was combined with exercise (see Table). These findings are indicative of the high level of reserve capacities of the SAS at the early stage of intermittent exposure to SMF, when intensified secretion of E in blood with exercise was apparently compensated by its intensified resynthesis. On the 30th day of exposure to SMF, after swimming, a sufficient reserve of both CA remained in the adrenals, and consequently the decrease in blood E concentration in these rats, as compared to the parameter for control animals, after swimming cannot be attributed to depletion of medullary layer function. In all probability, long-term repetition of exposure to SMF led to decrease in

Effect of exercise on CA level in rat adrenal after exposure to 1.6 T SMF

Experimental conditions	Number of rats	E, μg/g	NE, μg/g
Control	28	881,54±54,63	224,95±41,46
After swimming	27	796,04±57,94	217,53±23,31
1-5-fold exposure to SMF + swimming	16	912,22±71,18	333,22±54,12 $P<0,1$
15-fold exposure to SMF + swimming	10	921,04±50,10	336,60±76,18
30-fold exposure to SMF + swimming	10	873,20±46,73	264,76±38,81

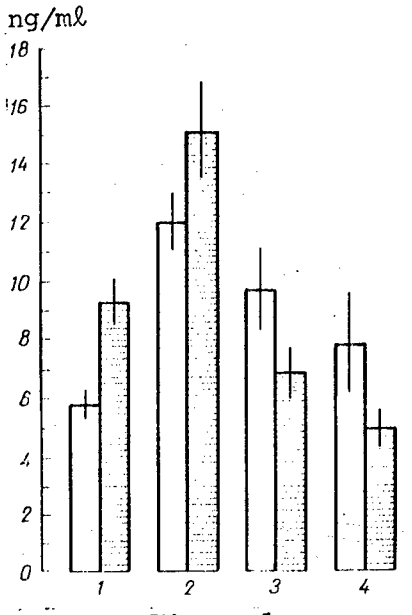

Figure 1.
Effect of physical load on blood E content in control rats and rats exposed to SMF with induction of 1.6 T daily for 3 h per day
1) control
2) 1-15 exposures to SMF
3) 30 exposures to SMF
4) 1 day after 30th exposure
White bars--without exercise, striped--after swimming. Y-axis, quantity of E (ng/mℓ)

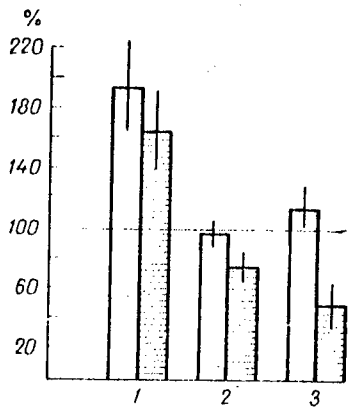

Figure 2.
Change (% of control) in maximum swimming time and blood E content in rats after swimming under the effect of 3-h daily exposure to SMF with induction of 1.6 T
1) 1-15 exposures to SMF
2) 30 exposures
3 1 day after 30 exposures
White bars--swimming time, striped--blood E content after swimming
Y-axis, value of relevant parameter (% of control)

in reactivity of the SAS, which diminished appreciably passage of E from the adrenals during swimming, while intensified utilization of the hormone due to exercise [1, 3] became the cause of its relative shortage in circulating blood.

Thus, tests with intensive exercise revealed two phases of functional changes in the SAS in the course of long-term intermittent exposure to a strong SMF. It

is important to mention that fluctuation of physical work capacity occurred synchronously with these phases. Figure 2 compares the effect of SMF on swimming time to the point of total fatigue and blood E level after swimming in the same rats.

The existence of a correlation between change in swimming time and level of SAS activity is indicative of the role of adrenergic mechanisms in expression of SMF effects on physical work capacity. This applies, first of all, to the stimulating effect observed at the first stage of exposure to SMF. The surplus of CA in the adrenals is one of the elements of the general adaptive reaction to a physical load [8].

With decline in SAS reactivity by the 30th day of exposure to SMF, there was a decrease in physical work capacity, as compared to the first stage. However, maximum swimming time did not decrease below control levels, although blood E content was considerably lower after swimming than in rats who only swam. Evidently, the intensified expenditure of hormone circulating in blood was instrumental in maintaining a normal physical work capacity. The changes observed in the second stage of exposure to SMF differ from the conditioning process with long-term repetition of moderate exercise, when metabolic and functional change in the SAS is aimed at enhancing physical work capacity [3, 8, 10, 11].

In conclusion, it must be stressed that such an integral indicator of adaptability as tolerance to maximum physical load after 30-fold exposure to SMF remained at the control level. The obtained data are indicative of a compensated state of adaptive systems following daily exposure for 3 h a day to a strong SMF for 1 month. However, they do not enable us to predict physical endurance in the case of exposure for more than 30 days to a high-intensity SMF.

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DIRECT AND INDIRECT EFFECTS OF STATIONARY MAGNETIC FIELD ON BIOLOGICAL SYSTEMS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 18 Jun 85) pp 73-76

[Article by T. P. Pantev and M. I. Minkova (People's Republic of Bulgaria)]

[English abstract from source] The effect of a constant magnetic field (CMF) of H = 2.3×10^5 A/m (2900 Oe) on the viability and radiosensitivity of E. coli B and the effect of magnetically activated water (MAW) on the radioresistance of rats were examined. The exposure did not influence the growth kinetics of E. coli B. Cell cultivation in the magnetically pretreated nutrient medium enhanced the bacterial growth. Preliminary exposure of bacterial cells to a CMF for 24 and 48 h increased and that for 72 h decreased their radioresistance. Twice a day the experimental weanlings were given MAW and the controls--tap water. The postradiation longevity of the MAW rats proved extended as compared to that of the controls. The MAW rats showed a higher osmotic stability of erythrocytes, a higher concentration of nucleic acids, and a larger count of leukocytes.

[Text] When solving problems of space biology and medicine, there is increased interest in the effects of a stationary magnetic field (SMF) on living organisms. During spaceflights, terrestrial biological systems may be either beyond the effect of the geomagnetic field or under conditions that exceeded by several times the usual geomagnetic background. In a physiological state, these systems present deviations that have not been sufficiently investigated [10, 11, 15, 18].

It should be noted that, along with the direct effect of a magnetic field (MF) on biological objects, there is also an indirect effect as a result of alteration of properties of water [7, 12]. Evidently, when using powerful MF aboard spacecraft, both intracellular water and water stored onboard are exposed to their effects. The indirect effect of SMF on physiological processes (that of so-called "magnetized" or magnet-activated water--MAW) has been demonstrated in several studies [1, 5, 7, 14].

Several studies revealed attenuation of radiation effects when objects were exposed to SMF [4, 11, 15-17].

Considering the multifacetted effects of SMF and MAW on various biological systems, our objective was to investigate their influence on the radiobiological effect of acute and chronic irradiation. The studies were pursued on Escherichia coli bacterial cells and on rats.

Methods

The direct and indirect effects of SMF on bacterial cells were tested in the following manner: E. coli strain B cells were cultured in an SMF of $(2-3)\cdot10^5$ A/m at 37°C. Culture development was monitored in the 1st, 3d, 4th, 5th and 24th h. In another experimental variant, the culture was inoculated on broth which had first been exposed for 18, 24 and 48 h to an SMF, and then they were cultivated outside an SMF. In the next series of experiments, bacterial suspensions were exposed to SMF for 24, 48 and 72 h at room temperature, then exposed to radiation in the dose range of 50-600 Gy. We determined the colony-forming capacity of cells 48 h later.

The indirect effect of SMF on rats was studied using MAW, to obtain which we passed tap water (10 m/s) between the poles of the same magnet. We conducted two series of experiments.

In the first series, we used brief exposure to x-rays in a lethal dosage. Animals weighing 52-54 g were divided into 2 groups of 11 animals in each: experimental, which was given MAW for 42 days, and control, which was given ordinary water. We changed the drinking water of both groups of animals twice a day and at equal intervals we checked weight gain. One week later, the animals were exposed to radiation in a dosage of 8.4 Gy from an x-ray therapy unit with the following parameters: 250 kV, 15 mA, 0.35 mm copper filter, target distance 50 cm, dose rate 0.96 Gy/min. After irradiation, the animals of both groups were given ordinary water, and we monitored their survival daily for 30 days.

The second series involved chronic irradiation. The experiment lasted 270 days. Ninety days after the start of MAW intake, 20 animals each from the experimental and control groups were exposed for 52 days to ^{226}Ra γ-rays at a dose rate of 0.01 Gy/h (0.23 Gy/day). Total dosage constituted 12 Gy. Just prior and immediately after irradiation, we determined body weight, osmotic resistance of red blood cells [8] and concentration of nucleic acids (NA) in peripheral blood leukocytes [9].

Results and Discussion

Exposure of a grown culture to SMF did not elicit statistically significant changes in kinetics of the growth cycle in E. coli B. Cultivation of cells in magnet-treated nutrient medium increased bacterial growth.

Pre-exposure of bacterial cells to an SMF altered significantly their response to radiation. A comparison of dose-effect curves for the control and a suspension exposed to SMF for 24 h revealed noticeable enhancement of radioresistance of exposed cells. As shown by quantitative analysis, a radiation dose of 600 Gy is absolutely lethal for intact cells. The same dosage did not elicit complete inactivation of colony-forming capacity in cells exposed to SMF. The results

of experiments performed to determine the effect of 2-day exposure of bacterial cells to SMF on their radiosensitivity also revealed that radioresistance of the strain was enhanced. However, 3-day exposure to SMF of a bacterial suspension led to distinct increase in radiosensitivity of cells.

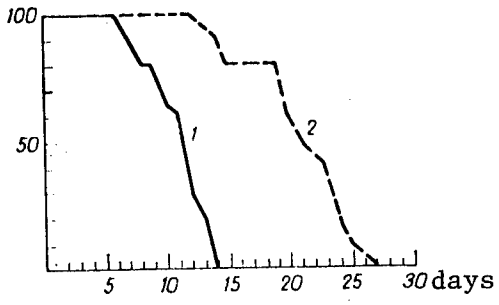

Figure 1.
Survival of control rats and animals given MAW after exposure to γ-radiation
Here and in Figures 2 and 3:
1) control animals
2) rats given MAW

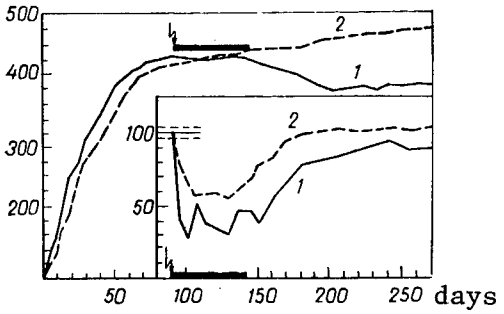

Figure 2.
Effect of MAW on weight and leukocyte count in rats before and after chronic γ-irradiation; y-axis, on the left--animals' weight (% of baseline), right--leukocytes (% of baseline); arrowhead indicates irradiation

Intake of MAW by rats for 42 days had a noticeable effect on dynamics of changes in mean body weight. This parameter rose more slowly in them than in control animals. Delivery of radiation in a dosage of 8.4 Gy was absolutely lethal for both groups (Figure 1). However, analysis of time of death revealed substantial differences in these parameters. Cases of radiation death began to appear in control animals on the 6th postradiation day and in experimental ones, on the 14th postradiation day. All control animals died by the 14th day, whereas rats given MAW died by the 26th day. In the control, most animals died between the 10th and 14th days, whereas among rats given MAW the maximum number of deaths was recorded on the 20th and 24th days.

The results of the second series of experiments (Figure 2) confirm the above findings and indicate that, even on the 90th day, experimental animals kept on MAW gained weight more slowly than control rats. Leukocyte count failed to demonstrate differences between the two groups for 90 days.

Chronic exposure to radiation for 52 days (from the 90th to 142d day of the experiment) at a low dose rate led to reduction of animals' weight. By the end of the course of radiation, there were statistically reliable differences between parameters of both groups (see Figure 2).

Peripheral blood parameters are also indicative of the beneficial effect of MAW in the case of chronic exposure to radiation. At all tested times from the start of irradiation to the end of the experiment, leukocyte count was significantly higher in the experimental group, and both the phase of abortive increase in number of leukocytes (10th-15th days) and secondary leukopenia were less marked (see Figure 2). By the 30th day after irradiation the number of leukocytes reverted to normal values in animals given MAW, whereas in the control there was incomplete recovery of leukocytes to the end of the observation period.

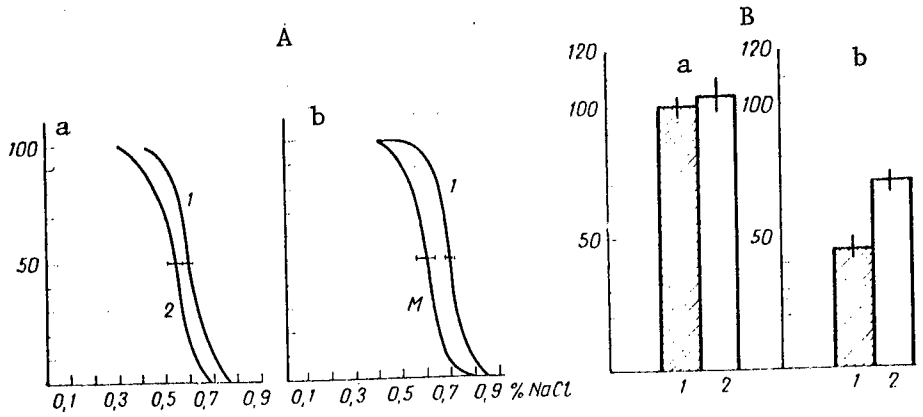

Figure 3. Changes in osmotic resistance of erythrocytes (A) and NA concentration in leukocytes (B) in intact rats (a) and those exposed to chronic radiation

Osmotic resistance of erythrocytes increased with statistical reliability in experimental rats who drank MAW (Figure 3Aa). Chronic irradiation (12 Gy) diminished erythrocyte resistance to hypotonic solution: there was a shift in hemolytic concentration of sodium chloride by a mean of 0.6 (0.58-0.62) to 0.7% (0.68-0.72). MAW raised this parameter from 0.55% (0.52-0.58) to 0.59% (0.56-0.62). Analogous changes were observed in iminimum and maximum resistance of red blood cells in the experimental and control groups (Figure 3Ab). According to the data from osmotic erythrograms, the curve of hemolytic resistance shifts to the right under the influence of MAW, which is indicative of prevalence of more stable cells in blood. In the case of chronic irradiation, there was prevalence of less stable erythrocytes in the blood of control rats. In irradiated animals given MAW, the erythrograms did not exceed the range of normal curves.

NA concentration in peripheral blood leukocytes of animals given MAW did not differ from that of control animals before irradiation (Figure 3Ba). With use of the model of chronic radiation, the radiation factor led to a decline of NA concentration in both groups of animals, and this decline was considerably more marked than in the control.

The results revealed that the direct effect of SMF does not affect growth of the bacterial E. coli strain. Prior "magnetic activation" of the liquid nutrient medium has a stimulating effect on development of the bacterial culture. Under certain conditions, SMF can elicit a radioprotective effect in E. coli B, and the e-tent of this effect is a function of duration of exposure. With increase in duration of exposure the protective effect of SMF decreases, and with long-term exposure the opposite effect is observed.

Long-term intake of MAW elicits some changes in the animals' condition. The slower mean weight gain in animals given MAW should be attributed to the fact, which was reported by Yu. A. Kholodov [14] and confirmed by other authors [3, 7, 11, 17], that MAW slows down oxidative processes in biological systems without affecting vital functions. Long-term intake of MAW elicits slower synthesis of ATP and, consequently, a state of chronic hypoxia [7, 14].

Although the death rate was the same in both groups of animals exposed to a lethal dose of x-rays, the later time of death of rats given MAW is indicative of the considerably more active compensatory mechanisms in these animals [3, 7]: mean survival time was 11.5 days in the control and 21 days in the experiment.

The increased erythrocyte resistance we observed in rats given MAW does not agree with some of the data in the literature [2, 12] which, however, were obtained after treatment of erythrocyte suspensions with SMF. The prevalence in our experiments of more stable erythrocytes in blood is probably due to destruction of unstable cell populations. There are reports [6, 13] of analogous results with exposure of animals to SMF, which reinforces the hypothesis of abscopal biomagnetic effect of MAW.

Enhancement of radioresistance of bacterial cells and animals as a result of long-term use of SMF and MAW in our experiments reinforces indirectly the conclusion of Yu. A. Kholodov concerning a decrease in rate of oxidative processes.

The findings warrant the conclusion that both the direct and indirect effect of SMF on living organisms elicits certain changes in their state which lead, in particular, to attenuation of radiation damage with use of moderate and sublethal doses of radiation.

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DERIVATION OF WORKING EQUATIONS OF CO_2-CO-H_2O-H_2-N_2 GAS MIXTURE FOR CATHODE SPACE OF ELECTROLYZER WITH SOLID ELECTROLYTE, WITH CONSIDERATION OF EXTRACTED OXYGEN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 4 Feb 85) pp 76-79

[Article by B. G. Grishayenkov, V. K. Vasilyev, N. G. Zorina and A. K. Zhukov]

[English abstract from source] Equations of thermodynamic equilibrium of the gas mixture CO_2-CO-H_2O-H_2-N_2 for the cathode space of the electrolyzer containing a solid electrolyte with extracted oxygen taken into consideration were derived. Equilibrium partial gas pressures, thermal effect of reactions, theoretical voltage of dissociation (the system of equations included 11 unknown parameters) were determined. These parameters are functions of temperature, total pressure of the gas mixture, initial gas composition, and the coefficient characterizing the degree of oxygen transfer from the cathode cell to the anode cell of the electrolyzer.

[Text] Let us designate the initial partial pressures of constituents in a CO_2-CO-H_2O-H_2-N_2 gas mixture as:

$$P^{00}_{CO_2},\ P^{00}_{CO},\ P^{00}_{H_2O},\ P^{00}_{H_2},\ P^{00}_{N_2}.$$

Total pressure π in the reaction chamber of an electrolyzer with solid electrolyte equals:

$$\pi = \sum_i P_i^{00} = P^{00}_{CO_2} + P^{00}_{CO} + P^{00}_{H_2O} + \\ + P^{00}_{H_2} + P^{00}_{N_2}. \quad (1)$$

The process of electrochemical dissociation of oxygen-containing molecules in an electrolyzer with solid electrolyte is characterized by the fact that the oxygen contained in the initial molecules of gas moves from the reaction chamber of the system to the oxygen chamber (anode). Thus, for each degree of passage

of oxygen (ν_n) there is an initial partial pressure of gas (P_i^0), with consideration of which one must determine thermodynamic equilibrium in the system under study: equilibrated partial pressures P_i, thermal effect of reactions Q_p and theoretical voltage of dissociation E_t. Parameters $\{P_i, E_t, Q_p\}$ are functions of temperature, overall pressure, initial composition of P_i^{00} and extent of transfer of oxygen ν_n.

The latter parameter is determine with consideration of the fact that there is no dissociation of CO_2 into C and O in the electrolyzer.

$$\nu_n = \frac{|O|^{00} - |O|^0}{|O|^{00} - |O|^*}, \tag{2}$$

where $|O|^{00}$ is atomic oxygen content in initial mixture, $|O|^0$ is atomic content of oxygen in the mixture corresponding to degree of transfer of oxygen ν_n, $|O|^*$ is atomic content of oxygen in the mixture corresponding to $\nu_n = 1$. By definition:

$$|O|^{00} = \frac{2P^{00}_{CO_2} + P^{00}_{CO} + P^{00}_{H_2O}}{3P^{00}_{CO_2} + 2P^{00}_{CO} + 3P^{00}_{H_2O} + 2P^{00}_{H_2}}, \tag{3}$$

$$|O|^0 = \frac{2P^{0}_{CO_2} + P^{0}_{CO} + P^{0}_{H_2O}}{3P^{0}_{CO_2} + 2P^{0}_{CO} + 3P^{0}_{H_2O} + 2P^{0}_{H_2}}, \tag{4}$$

$$|O|^* = \frac{P^{00}_{CO} + P^{00}_{CO_2}}{2\pi} = \frac{P^{00}_{CO} + P^{00}_{CO_2}}{2P^*_{CO} + 2P^*_{H_2}} =$$

$$= \frac{P^0_{CO}}{2P^*_{CO} + 2P^*_{H_2}}. \tag{5}$$

Equilibrated partial pressures of components P_i are related by equations of thermodynamic equilibrium of reactions of dissociation of H_2O into H_2 and O_2, and of CO_2 into CO and O_2:

$$K_1 P_{H_2O} = P_{H_2} \cdot P^{1/2}_{O_2}, \tag{6}$$

$$K_2 P_{CO_2} = P_{CO} \cdot P^{1/2}_{O_2} \tag{7}$$

and Dalton's equation:

$$\pi = \sum_i P_i = P_{CO_2} + P_{CO} + P_{O_2} + P_{H_2O} + P_{H_2}. \tag{8}$$

To solve this problem we must consider the equation that ensues from constancy of the [C/H] ratio for all ν_n and [O/C+H] for a given ν_n.

$$[C/H] = \frac{P^{00}_{CO_2} + P^{00}_{CO}}{2P^{00}_{H_2} + 2P^{00}_{H_2O}} =$$

$$= \frac{P^{0}_{CO_2} + P^{0}_{CO}}{2P^{0}_{H_2} + 2P^{0}_{H_2O}} = \frac{P_{CO_2} + P_{CO}}{2P_{H_2} + 2P_{H_2O}}, \quad (9)$$

$$[O/C + H] = \frac{P^{0}_{CO} + P^{0}_{H_2O} + 2P^{0}_{CO_2}}{P^{0}_{CO} + P^{0}_{CO_2} + 2P^{0}_{H_2} + 2P^{0}_{H_2O}} =$$

$$= \frac{P_{CO} + P_{H_2O} + 2P_{CO_2} + 2P_{O_2}}{P_{CO} + P_{CO_2} + 2P_{H_2} + 2P_{H_2O}}. \quad (10)$$

At the same time, it is obvious that:

$$[O/C + H]^0 \neq [O/C + H]^{00}, \quad (11)$$

since

$$[O/C + H]^0 = f([O/C + H]^{00}, \nu_n). \quad (12)$$

We find this function proceeding from:

$$[O/C + H]^0 = [O/C + H]^{00} \text{ at } \nu_n = 0, \quad (13)$$

$$[O/C + H]^0 = \frac{\pi - P^{00}_{H_2} - P^{00}_{H_2O}}{\pi + P^{00}_{H_2} + P^{00}_{H_2O}} \text{ at } \nu_n = 1. \quad (14)$$

According to equations (13) and (14):

$$[O/C + H] = \frac{\nu_n(\pi - P^{00}_{H_2} - P^{00}_{H_2O})}{\pi + P^{00}_{H_2} + P^{00}_{H_2O}} + (1 - \nu_n)[O/C + H]^{00} \quad (15)$$

or

$$\frac{P^{0}_{CO} + P^{0}_{H_2O} + 2P^{0}_{CO_2}}{P^{0}_{CO} + P^{0}_{CO_2} + 2P^{0}_{H_2} + 2P^{0}_{H_2O}} = \frac{\nu_n(\pi - P^{00}_{H_2} - P^{00}_{H_2O})}{\pi + P^{00}_{H_2} + P^{00}_{H_2O}} + \frac{(1 - \nu_n)(P^{00}_{CO} + P^{00}_{H_2O} + 2P^{00}_{CO_2})}{P^{00}_{CO} + P^{00}_{CO_2} + 2P^{00}_{H_2O} + 2P^{00}_{H_2}}. \quad (16)$$

This equation was obtained on the assumption that function (12) is linear and approximate. In cases where P^0_i is a substantial function of temperature, one must use the equation of thermodynamic equilibrium for water gas reaction, instead of equation (16):

$$\frac{K_2}{K_1} = \frac{P^0_{CO} \cdot P^0_{H_2O}}{P^0_{CO_2} \cdot P^0_{H_2}}. \qquad (17)$$

Theoretical voltage of dissociation is calculated using the well-known formula:

$$E_t = 0{,}049599 \cdot T \cdot \lg \frac{P_{O_2}}{\bar{P}_{O_2}} \qquad [1].$$

In calculating thermal effect $\bar{Q}_p$ of the process for a given ν_n characterizing the $P^{00}_i \to P^0_i$, let us examine the stoichiometry of this conversion:

$$\begin{aligned}
&\left(P^{00}_{H_2O}\right)_{H_2O} + \left(P^{00}_{CO_2}\right)_{CO_2} + \left(P^{00}_{CO}\right)_{CO} + \\
&+ \left(P^{00}_{H_2}\right)_{H_2} = \left(P^0_{H_2O}\right)_{H_2O} + \left(P^0_{CO_2}\right)_{CO_2} + \\
&+ \left(P^0_{CO}\right)_{CO} + \left(P^0_{H_2}\right)_{H_2} + 0{,}5P^{00}_{H_2O} + P^{00}_{CO_2} + \\
&+ 0{,}5P^{00}_{CO} - 0{,}5P^0_{H_2O} - P^0_{CO_2} - \\
&- 0{,}5P^0_{CO})_{O_2} + \pi\bar{Q}_p.
\end{aligned} \qquad (18)$$

In accordance with the law of Hess, total thermal effect is:

$$\bar{Q}_p = \bar{Q}^1_p + \bar{Q}^2_p, \qquad (19)$$

where $\bar{Q}^1_p$ and $\bar{Q}^2_p$ are thermal effects of conversions:

$$\begin{aligned}
\left(P^{00}_{H_2O} - P^0_{H_2O}\right)_{H_2O} &= \left(P^0_{H_2} - P^{00}_{H_2}\right)_{H_2} + \\
&+ \left(0{,}5P^{00}_{H_2O} - 0{,}5P^0_{H_2O}\right)_{O_2} + \pi\bar{Q}^1_p,
\end{aligned} \qquad (20)$$

$$\begin{aligned}
\left(P^{00}_{CO_2} - P^0_{CO_2}\right)_{CO_2} &= \left(P^0_{CO} - P^{00}_{CO}\right)_{CO} + \\
&+ \left(P^{00}_{CO_2} + 0{,}5P^{00}_{CO} - P^0_{CO_2} - \right. \\
&\left. - 0{,}5P^0_{CO}\right)_{O_2} + \pi\bar{Q}^2_p.
\end{aligned} \qquad (21)$$

According to equations (19)-(21):

$$\begin{aligned}
\pi\bar{Q}_p = &- \Delta H_1 \left(P^{00}_{H_2O} - P^0_{H_2O}\right) - \\
&- \Delta H_2 \left(P^{00}_{CO_2} - P^0_{CO_2}\right),
\end{aligned} \qquad (22)$$

Thus, we have the following system of equations:

$$
\begin{gathered}
K_1 P_{H_2O} = P_{H_2} \cdot P_{O_2}^{1/2}; \\
K_2 P_{CO_2} = P_{CO} \cdot P_{O_2}^{1/2}; \\
\pi = P_{CO_2} + P_{CO} + P_{O_2} + P_{H_2O} + P_{H_2} + P_{N_2}^{00}; \\
\pi = P_{CO_2}^0 + P_{CO}^0 + P_{H_2O}^0 + P_{H_2}^0 + P_{N_2}^{00} \\
\nu_n = \frac{\frac{2P_{CO_2}^{00}+P_{CO}^{00}+P_{H_2O}^{00}}{3P_{CO_2}^{00}+2P_{CO}^{00}+3P_{H_2O}^{00}+2P_{N_2}^{00}+2P_{H_2}^{00}} - \rightarrow}{\frac{2P_{CO_2}^{00}+P_{CO}^{00}+P_{H_2O}^{00}}{3P_{CO_2}^{00}+2P_{CO}^{00}+3P_{H_2O}^{00}+2P_{H_2}^{00}+2P_{N_2}^{00}} -} \\
\rightarrow \frac{\frac{2P_{CO_2}^0+P_{CO}^0+P_{H_2O}^0}{3P_{CO_2}^0+2P_{CO}^0+3P_{H_2O}^0+2P_{H_2}^0+2P_{N_2}^{00}}}{\frac{P_{CO}^{00}+P_{CO_2}^{00}}{2\pi}}. \\
\frac{P_{CO_2}^{00}+P_{CO}^0}{P_{H_2}^{00}+P_{H_2O}^{00}} = \frac{P_{CO_2}^0+P_{CO}^0}{P_{H_2}^0+P_{H_2O}^0}; \\
\frac{P_{CO_2}^{00}+P_{CO}^{00}}{P_{H_2}^{00}+P_{H_2O}^{00}} = \frac{P_{CO_2}+P_{CO}}{P_{H_2}+P_{H_2O}}; \\
\frac{P_{CO}^0+P_{H_2O}^0+2P_{CO_2}^0}{P_{CO}^0+P_{CO_2}^0+2P_{H_2O}^0+2P_{H_2}^0} \\
= \frac{P_{CO}+P_{H_2O}+2P_{CO_2}+2P_{O_2}}{P_{CO}+P_{CO_2}+2P_{H_2}+2P_{H_2O}}; \\
K_2/K_1 = \frac{P_{CO}^0 \cdot P_{H_2O}^0}{P_{CO_2}^0 \cdot P_{H_2}^0}; \\
E_t = 0{,}049599T \lg \frac{P_{O_2}}{\overline{P}_{O_2}}; \\
\pi Q_p = -\Delta H_1 \left(P_{H_2O}^{00} - P_{H_2O}^0\right) - \\
-\Delta H_2 \left(P_{CO_2}^{00} - P_{CO_2}^0\right).
\end{gathered}
\tag{23}
$$

The system of equations (23) is solved for 11 unknown parameters:

$$
P_{H_2O},\ P_{CO_2},\ P_{H_2},\ P_{CO},\ P_{O_2},\ P_{H_2O}^0,\ P_{H_2}^0,
$$
$$
P_{CO_2}^0,\ P_{CO}^0,\ E_t,\ Q_p.
$$

The following values are given: π, T (consequently,

$$
K_1 K_2 \Delta H_1 \Delta H_2),\ P_{CO_2}^{00},\ P_{CO}^{00},\ P_{H_2O}^{00},\ P_{H_2}^{00},\ P_{N_2}^{00},
$$
$$
\nu_n,\ \overline{P}_{O_2}.
$$

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UDC: 629.78.063.:574.685

CALCULATION OF EQUILIBRATED CONCENTRATIONS OF CONSTITUENTS OF CO_2-CO-H_2O-H_2-N_2 GAS MIXTURE FOR CATHODE SPACE OF ELECTROLYZER WITH SOLID ELECTROLYTE AND CORRESPONDING VALUES OF THEORETICAL VOLTAGE OF DISSOCIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 4 Feb 85) pp 79-81

[Article by B. G. Grishayenkov, N. G. Zorina and V. K. Vasilyev]

[Text] Analysis of working equations of thermodynamic equilibrium of a CO_2-CO-H_2O-H_2-N_2 gas mixture in the cathode space of an electrolyzer with solid electrolyte, written in the form rendered on the next page, amounts to solution of algebraic equations that are nonlinear in relation to $P^0_{H_2O}$, $P^0_{CO_2}$, P^0_{CO} and $P^0_{H_2}$, which can be rendered in the following equivalent form:

$$F(x, \alpha, K) = 0$$

where $x(x_1 \ldots x_9)$ are the sought parameters (P_i, P^0), $\alpha(\alpha_1 \ldots \alpha_m)$ are fixed parameters determined by initial concentrations of constituents P^{00}_i, stoichiometric coefficients, pressure π and a coefficient characterizing the degree of passage of oxygen from the cathode chamber of the electrolyzer into the anode chamber ν_n. $K(K_1, K_2)$ are constants of equilibrium of the corresponding reactions, $F(F_1 \ldots F_9)$ is specified vector function.

Calculation of equilibrated concentrations of elements of the gas mixture in question and corresponding theoretical voltage of dissociation was made on a digital computer using the ALGOL-60 computer language, for temperatures of 1000-1400°K and coefficients ν_n of migration of oxygen, which changed from 0 to 1. We specified the following initial concentrations of mixture constituents:

$$P^0_{H_2O}=0,2;\ P^0_{CO}=0,8;\ P^0_{H_2O}=0,4;\ P^0_{CO_2}=0,6;$$
$$P^0_{H_2O}=0,6;\ P^0_{CO_2}=0,4;\ P^0_{H_2O}=0,8;\ P^0_{CO_2}=0,2.$$

To check the calculations for a system with initial concentrations of constituents of the gas mixture from 0.2 to 0.8 molar parts of H_2O mixed with CO_2, we calculated some of the mean points characterized by presence of a four-component mixture: CO_2, CO, H_2O, H_2.

Working equations:

$$K_1 P_{H_2O} = P_{H_2} \cdot P_{O_2}^{1/2}$$

$$K_2 P_{CO_2} = P_{CO} \cdot P_{O_2}^{1/2}$$

$$\pi = P_{CO_2} + P_{CO} + P_{O_2} + P_{H_2O} + P_{H_2} + P_{N_2}^{00}$$

$$\pi = P_{CO_2}^0 + P_{CO}^0 + P_{H_2O}^0 + P_{H_2}^0 - P_{N_2}^{00}$$

$$\nu_n = \frac{\frac{2P_{CO_2}^{00}+P_{CO}^{00}+P_{H_2O}^{00}}{3P_{CO_2}^{00}+2P_{CO}^{00}+3P_{H_2O}^{00}+2P_{H_2}^{00}+2P_{N_2}^{00}} - \frac{2P_{CO_2}^{0}+P_{CO}^{0}+P_{H_2O}^{0}}{3P_{CO_2}^{0}+2P_{CO}^{0}+3P_{H_2O}^{0}+2P_{H_2}^{0}+2P_{N_2}^{00}}}{\frac{2P_{CO_2}^{00}+P_{CO}^{00}+P_{H_2O}^{00}}{3P_{CO_2}^{00}+2P_{CO}^{00}+3P_{H_2O}^{00}+2P_{H_2}^{00}+2P_{N_2}^{00}} - \frac{P_{CO}^{00}+P_{CO_2}^{00}}{2\pi}}$$

$$\frac{P^{00}CO_2 + P_{CO}^{00}}{P^{00}H_2 + P^{00}H_2O} = \frac{P^0CO_2 + P_{CO}^0}{P^0H_2O + P^0H_2}$$

$$\frac{P^{00}CO_2 + P_{CO}^{00}}{P^{00}H_2 + P^{00}H_2O} = \frac{P_{CO_2} + P_{CO}}{P_{H_2} + P_{H_2O}}$$

$$\frac{P_{CO}^0 + P_{H_2O}^0 + 2P_{CO_2}^0}{P_{CO}^0 + P_{CO_2}^0 + 2P_{H_2O}^0 + 2P_{H_2}^0} =$$

$$= \frac{P_{CO} + P_{H_2O} + 2P_{CO_2} + 2_{PO_2}}{P_{CO} + P_{CO_2} + 2P_{H_2} + 2P_{H_2O}}$$

$$K_2/K_1 = \frac{P_{CO}^0 \cdot P_{H_2O}^0}{P_{CO_2}^0 \cdot P_{H_2}^0}$$

$$E_t = 0{,}049599 \cdot T \cdot \lg P_{O_2}/P_{O_2}$$

$$\pi\theta_p = -\Delta H_1 \left(P_{H_2O}^{00} - P_{H_2O}^0\right) - \\ -\Delta H_2 \left(P_{CO_2}^{00} - P_{CO_2}^0\right)$$

Figure 1 illustrates an example of theoretical voltage of dissocation E_t as a graphic function of oxygen content in the mixture [0/C+H] or ν_n and the corresponding concentrations of constituents of the gas mixture at temperatures of 1000-1400°K.

The Table lists values characterizing the tested gas mixtures: $[H/C]^{00}$ ratio, oxygen content [0/C+H] and corresponding coefficients that determine the extent of oxygen transfer ν_n from the cathode chamber of the electrolyzer to the anode chamber.

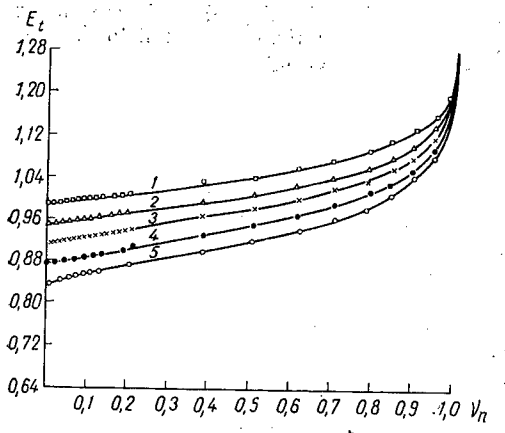

Figure 1.

Plots of theoretical dissociation voltage E_t and partial pressures of gas mixture constituents as function of oxygen transfer ν_n for mixtures with initial concentrations of constituents $P^0_{CO_2} = 0.8$; $P^0_{H_2O} = 0.2$ for the temperature range of 1000-1400°K

1-5) temperatures of 1000, 1100, 1200 and 1400°K, respectively [sic]

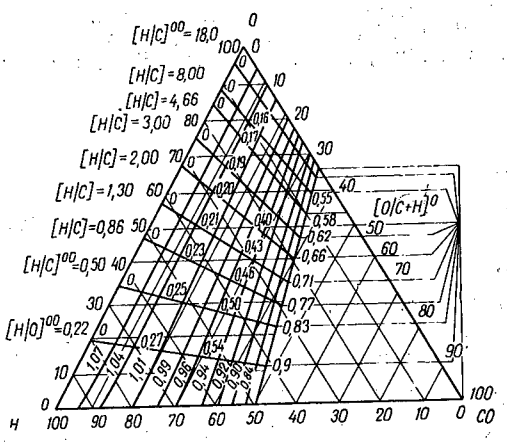

Figure 2.

Nomogram for determination of theoretical voltage of dissociation E_t of CO_2-CO-H_2O-H_2-N_2 gas mixture with different initial partial pressures of constituents $[H/C]^{00}$ and oxygen content $[O/C+H]^0$ for an electrolyzer temperature of 1000°K

According to the table, the concentrations of substances characterizing each of the mixtures under study can be expressed in the form of H:C:O ratios. In such such triple ratio, with fixed initial concentrations of constituents, there will be a change (decrease) in share of atoms of oxygen, the extent of loss of which can be characterized by the ratio, O/C+H. At the same time, for each fixed value of initial concentration of mixture constituents the H/C ratio remains constant. Thus, with each fixed value of H/C, the value of O/C+H, which characterizes oxygen content of a given gas mixture, changes from maximum to minimum.

List of parameters characterizing the gas mixtures under study

$[H/C]^{00}$	$[O/C+H]^0$	ν_n									
		0,1	0,2	0,3	0,4	0,5	0,6	0,7	0,8	0,9	1,0
0,22	0,90	081	072	063	054	045	036	027	018	009	0
0,50	0,83	075	066	058	050	042	033	025	017	008	0
0,86	0,77	069	062	054	046	038	031	023	015	0077	0
1,30	0,71	064	057	050	043	036	028	021	014	007	0
2,00	0,66	059	053	046	040	033	026	020	013	0066	0
3,00	0,62	056	050	043	037	031	025	019	012	0062	0
4,66	0,58	052	046	041	035	029	023	017	012	0058	0
8,00	0,55	050	044	038	033	028	022	016	011	0055	0
18,0	0,52	047	042	036	031	026	021	016	010	0052	0

It is known that a system of coordinates with a triangular equilateral base (Gibbs triangles) can be used to determine the properties of different mixtures characterized by presence of three heterogeneous atoms. Triangles of this type have the following distinctions: each point within a triangle has three positve

coordinates, the sum of which equals the perimeter of the triangular system; each point situated on one of the sides of the triangle has one coordinate that equals zero; all points situated on a line parallel to one of the sides of the triangle have the same coordinate, the one that this line cuts on the side of the triangle (clockwise direction from the side of the triangle to which the line is parallel); if a line is drawn through the apex of the triangle, it will constitute the geometric site of points with equal relationship to two homologous coordinates.

In this case, we can take parameters H, CO and O with a range of changes from 0 to 100% as the base of the chosen triangular system of coordinates. Each of the gas mixtures studied is characterized by a specific $[H/C]^{00}$ ratio (see Table). On the selected triangular nomogram, the $[H/C]^{00}$ ratio is the geometric site of points, a straight line. Each point on the line is characterized by its own oxygen content $[O/C+H]^{0}$ or degree of oxygen transfer ν_n and corresponding theoretical voltage of dissociation E .

Figure 2 illustrates a nomogram describing the state of a CO_2-CO-H_2O-H_2 N_2 gas mixture for a temperature of 1100°K [sic--does not agree with figure caption].

Thus, calculation of thermodynamic equilibrium of a CO_2-CO-H_2O-H_2-N_2 gas mixture in the cathode space of an electrolyzer with solid electrolyte shows that theoretical voltage of dissociation of gas mixture E_t as a function of oxygen content of the mixture $[O/C+H]$ - (ν_n) is represented by S-shaped curves for all tested temperatures. Elevation of electrolyzer temperature shifts the curves in the direction of decline of theoretical dissociation voltage, without changing their appearance. An increase in $[H/C]^{00}$ causes insignificant shift (0.018 V) of theoretical dissociation voltage at all tested temperatures.

BRIEF REPORTS

UDC: 616.65+617.555/.559]-005-092:612.014.447-063

SOME PATHOLOGICAL SIGNS IN PELVIS MINOR ORGANS AFTER EXPOSURE TO LONG-TERM HIGH-LEVEL +Gz ACCELERATIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 9 Jun 86) pp 81-82

[Article by A. S. Barer, A. A. Okhobotov, Ye. I. Sorokina and V. M. Tardov]

[Text] Circulatory conditions in the region of the hunan pelvis minor can be described as follows when performing maneuvers on modern aircraft involving long-term accelerations of high levels. In the presence of an increasing hydrostatic component of blood pressure reaching about 27-32 kPa with 9 G accelerations, the antigravity gear effects compensatory mechanical compression of the anterior abdominal wall and lower extremities, forcing up to 700 cc blood from leg vessels to areas above them, which should ultimately lead to marked increase in blood volume expressly in the pelvic region. In turn, this circumstance and the related elevation of transmural pressure could lead to pathological symptoms as a reuslt of increased permeability of the vascular wall under such conditions, and in some cases to its injury. In addition, these hemodynamic changes can elicit a set of symptoms inherent in static phenomena, i.e., impairment of transport functions of blood, edema, etc.

Since the question of possibility of pathological symptoms referable to pelvic organs has been virtually overlooked in the literature, our objective was to investigate these phenomena. We chose the prostate as the object of our study, since it is topographically situated in the region of maximum mechanical effect, and it is accessible to palpatory examination, while its secretions can be submitted to morphological laboratory analysis.

We screened 5 men 20 to 38 years of age who presented no pathological deviations in a background urological examination.

As a result, we obtained the following data. Palpatory examination of the prostate immediately after centrifuge testing with exposure to a complicated profile of 2-9 G accelerations, signs of edema were demonstrated in 3 out of 9 cases, and they were associated with atonia or consolidation of the gland along the periphery. Morphological analysis of prostate secretions revealed fresh erythrocytes in 8 out of 9 cases, up to 12 per field. The severity of these symptoms was a function of intensity of accelerations, as well as how the lower limbs were compressed. In addition, it was of some interest to find that, along with

edema of the prostate, there was swelling of hemorrhoidal nodes in a number of cases.

Thus, already the first specific investigation revealed that adverse symptoms related to increased delivery of blood to organs of the pelvis minor can develop in the vascular system and, consequently, in organs situated in the region of the pelvis minor under the effect of high-level and prolonged accelerations with concurrent compensatory compression of the lower limbs and anterior abdominal wall. In view of the clinical significance of the demonstrated phenomena, it is desirable to continue investigation of this matter from the standpoint of both diagnosis and development of a set of preventive measures.

UDC: 629.78:612.821.3.014.49

GROUP DYNAMICS AND PERFORMANCE EFFICIENCY UNDER EXTREME CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 18 Oct 85) pp 82-83

[Article by Jan Tereljak (Polish People's Republic)]

[Text] When psychologists analyze the process of social and emotional group dynamics of a small group spending the winter in Antarctica, they pay attention to the dynamics of psychophysiological responses related to this process. The behavioral disturbances discovered by a number of authors, which are elicited by long-term natural isolation, form the so-called "wintering syndrome" [6]. The most frequent manifestations of this syndrome are depression, hostility, irritability, impaired sleep, loss of interest in one's job, diminished intellectual capacities and interests [5]. These signs are related to the duration of the stay in an isolated group, monotony of the environment (monotony, boredom) and absence of customary emotional stimuli.

Analogous distinctions were also noted in many laboratory studies simulating spaceflight conditions, as well as during long-term spaceflights.

Dynamics of aggressive behavior. Our year-long studies of polar workers at the Polish Arttstovskiy Station (Buss-Durkee scale) established that as isolation progresses there is an increase in tendency toward aggressive behavior.

The highest indicator of physical aggressiveness was noted in the middle of the isolation period. This indicates that winter is the most difficult period for adjustment to a monotonous situation. The highest mark for verbal aggression noted in the last period indicates that a prolonged lack of exogenous stimuli is associated with mental discomfort and leads to fatigue (diminished control of one's behavior). It should be assumed that aggressive behavior compensates for the chronic shortage of stimuli [1, 4].

Dynamics of mental efficiency of the group. We used the Kraepelin test (lasting 1 h) to determine the dynamics of mental activity. Tests were made in cycles at 2-month intervals. We conducted a total of seven studies (one before the expedition and six in the course of year-long antarctic isolation). The subject's task was to continuously add numbers making marks (in response to a cue) of 3-min work periods. The marked segments were used to plot a curve which characterized variability of speed of mental work in the course of an hour.

We analyzed the total [3] number of operations and percentile change in rate of mental work from the first to the last periods of work--percentage of increment determines the level of overall mental endurance. Like Soviet authors [4], we failed to demonstrate worsening of mental performance, but we did observe development of fatigue, which is indicative of the nonspecific nature of decline of mental efficiency and, judging from all factors, it is related to sensory deprivation and monotony [2, 3].

Dynamics of informal group structure. A number of dynamic factors, which depend not only on working conditions and problems solved by the group, but on personality distinctions of its members, affect the quality of performance of any group, particularly a small one.

There is a system of formal and informal interpersonal relations in a group. While the former are determined by the position held by members, the latter are related to the psychological climate, atmosphere of friendship, mutual aid and other factors.

A number of authors stress the fact that, in small groups, there is most expressive manifestation of informal structure of relations, which has such a strong influence on group performance that it sometimes also alters the formal relations between people, influencing the quality of their group actions.

A group becomes a team only when the members have and are aware of a goal of their work, when they have the knowledge, abilities and skills that have been formed through experience, which are necessary to group work, as well as the capacity to maintain group unity. In a real group, there are usually functional pyschological mechanisms that compensate for the lack of intellectual and emotional unity. Knowledge of the dynamics of these mechanisms during long-term social isolation is the purpose of social space psychology.

One of the most important distinctions of small groups is psychological compatibility of its members. This concept takes into consideration mutual adaptation of group members to one another during work (and other forms of contact), interpersonal emotional ties based on love--nonlove relations, achievement of rapid and complete mutual understanding, personal and general readiness of group members for joint work, community of purposes and motivation for actions. In the presence of compatibility, a small group readily implements joint activity and is capable of functioning efficiently under difficult conditions in the course of prolonged isolation.

A study of the informal sociometric structure of the group of polar workers at the Polish Arttstovskiy Station, on the basis of the sympathy--antipathy criterion [7], made it possible to distinguish a typology of examples of social adaptation. The "conservative type" of adaptation is characterized by relatively constant good position on the approval scale throughout the period of isolation.

The "fluctuating type" is characterized by an element of cycles of changes in positions on the approval scale. This type of adaptation is inherent in individuals who demonstrate their independence from the group and periodically remain outside the group.

The "deadaptation type" is characterized by major changes in social adaptation. Most often, this is related to diminished prestige (judgment component) or sympathy (emotional component).

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UDC: 612.13-06:612.275

MECHANISM OF ACTION OF LOCAL NEGATIVE PRESSURE APPLIED TO HUMAN BODY ON DYNAMICS OF CENTRAL CIRCULATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 24 Sep 85) pp 84-86

[Article by V. V. Rumyantsev and A. I. Dyachenko]

[Text] Researchers are very interested in the effects of local negative (subatmospheric) pressure on the human body because of its extensive use in both space medicine and clinical practice. Use of lower body negative pressure (LBNP) is well-known as a means of preventing the adverse effect of weightlessness on man and as a functional test to evaluate resistance of the circulatory system to gravity factors after spaceflights. Other methods of local decompression have been studied less. We shall deal here with demonstration of the main factors that determine the response of central circulation to local negative pressure (LNP) on healthy man.

Methods

Healthy men who had undergone a thorough medical examination participated in this study. Central venous pressure (CVP) and pressure in the pulmonary artery (PPA) were measured by invasive methods. The entire lower half of the body, ankle and abdominal regions were submitted to 0 to -60 mm Hg negative pressure. The tests were made in the 20th min of head-down tilt (-15°). The methodological procedures, equipment used and primary data were submitted in greater detail in previous works [3, 4].

Results and Discussion

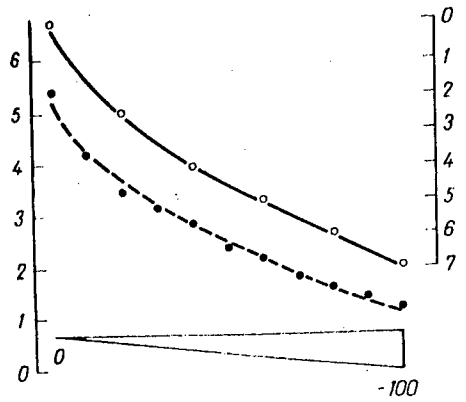
It was shown that both PPA and CVP are exponential functions of decompression level [5]. This function can be expressed in the form of an equation:

$$P = P_o + (P_b - P_o)\exp(Kp) \quad (1)$$

where P is PPA or CVP (in mm Hg), p is extent of decompensation (mm Hg), P_b is baseline pressure (mm Hg), P_o is end (minimum) pressure (mm Hg) and K is a coefficient.

With change in decompression mode (over the entire range), CVP and PPA become stabilized within as few as 15-20 s. This finding had been reported previously

by researchers for CVP [8]. During exposure to LNP, the crural volume is stabilized in 1 min [7]. It can be assumed that, in this situation, the change in CVP is attributable mainly to change in amount of excessively deposited blood in the decompressed region. In a test of the effects of LNP, it was established that rapid reduction of the end load level leads to the same result as stepped reduction [8].



Changes in CVP (dot-dash line; our findings) and crural volume (solid line, according to [7], as a function of level of decompression applied to ankle region (mean data for group, n = 6)
X-axis, decompression (mm Hg);
y-axis (left) CVP (mm Hg),
(right) ΔV (%)

Vein capacity is the most sensitive parameter in the case of relatively low degrees of decompression [1, 2]. Within a certain range, circulating blood volume (CBV) and CVP are considered to be linked by a linear function [6]. Duration is considered the only limiting factor (i.e., the changes occur rather rapidly). A linear function is applicable for both time and range of changes in CVP in our studies.

It can be assumed that processes occurring in the decompressed region are the cause of nonlinearity between CVP and degree of decompression. This can be validated by the fact that for the circulatory system as a whole the LNP used was low (linear reaction), whereas for the decompression zone it was significant (nonlinear reaction).

Thus, we observe the following sequence of changes under the effect of local decompression: decompression-transmural pressure-volume of veins-CBV-CVP.

We proposed the following model of the mechanism of action of decompression on the vascular bed--surrounding tissue system.

As we know, vessels become less elastic as they stretch. Let us assume that with decompression p the effective elasticity of vessels C (we are referring to venous vessels in soft tissues, which is essentially a vessel-surrounding tissue system) is a linear function of vascular volume V:

$$C = dV/dp = C_o - KV \qquad (2)$$

This applies to vessels that have already straightened out. The existing data warrant the conclusion that they do so with decompression of -10 to -15 mm Hg [4].

It is apparent from equation (2) that in a system with homogeneous properties parameter K does not depend on baseline volume of subsystem V_b (with p = 0), while C_o is proportionate to V_b. From equation (2) we derive the following:

$$V = V_o + (V_b - V_o)\exp(Kp) \qquad (3)$$

where $V_o = C_o/K$.

Comparative model parameters with exposure of ankle regions to LBNP and LNP

Subject	LBNP			LNP		
	P_o, mm Hg	P_b-P_o, mm Hg	100 K, $(mm\ Hg)^{-1}$	P_o, mm Hg	P_b-P_o, mm Hg	100 K, $(mm\ Hg)^{-1}$
P.	0	13,64	3,43	0	13,68	1,22
M.	0,32	15,07	4,01	7,04	8,12	2,25
D.	4,35	10,63	4,94	8,91	4,15	4,06
K.	1,78	10,44	6,71	5,4	4,45	2,07
S.	4,45	18,06	8,00	6,72	6,28	3,35
G.	3,96	14,15	3,81	9,1	6,07	2,21

The increase in vessel volume under the effect of decompression by dV alters CVP by dP:

$$V = V_o + (V_b - V_o)\exp(Kp) \text{ [repeat of (3)]} \qquad (4)$$

where X_{CB}* is the coefficient of CVP sensitivity to change in CBV.

Equations (2)-(4) are reduced to equation (1) with $P_o = P_b - X_{CB}V_bC_b/K$. Thus, the parameters of equation (1) acquire the following meaning. K characterizes effective elasticity as a function of volume, and it does not depend on V_b. P_b-P_o, which determines efficacy of decompression, is proportionate to baseline volume V_b, specific elasticity C_b and coefficient of sensitivity X_{CB}.

We used the data submitted by Coles et al. [7]. Plethysmography was used to measure increment in crural volume at decompression levels of -20 to -100 mm Hg at 20 mm Hg intervals. The data are illustrated in the Figure. Next to them is the curve of CVP as a function of decompression level [3]. Evidently, the changes in crural volume can be described by equation (3), and these changes are attributable mainly to elasticity parameter K. Thus, one can readily determine one of the main parameters of the model by an indirect method, by measuring volume increase in the decompression zone. The Table lists values for the parameters.

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*Translator's note: Obviously, equation (4) was omitted with (3) repeated in its place.

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RAT BRAIN POLYAMINE LEVELS DURING LONG-TERM HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 19 Dec 85) pp 86-87

[Article by V. Yu. Kovalev and R. A. Tigranyan]

[Text] Hypokinesia leads to changes in various aspects of metabolic processes [2, 3]. Polyamines, which include putrescine, spermidine and spermine, are considered to be indicators of intensity of protein biosynthesis [9], since they stimulate it on the level of DNA transcription [8, 10]. There are no data in the literature concerning involvement of polyamines in processes of adaptation to hypokinesia. We investigated here the levels of polyamines in different parts of the rat brain as related to different durations of hypokinesia.

Methods

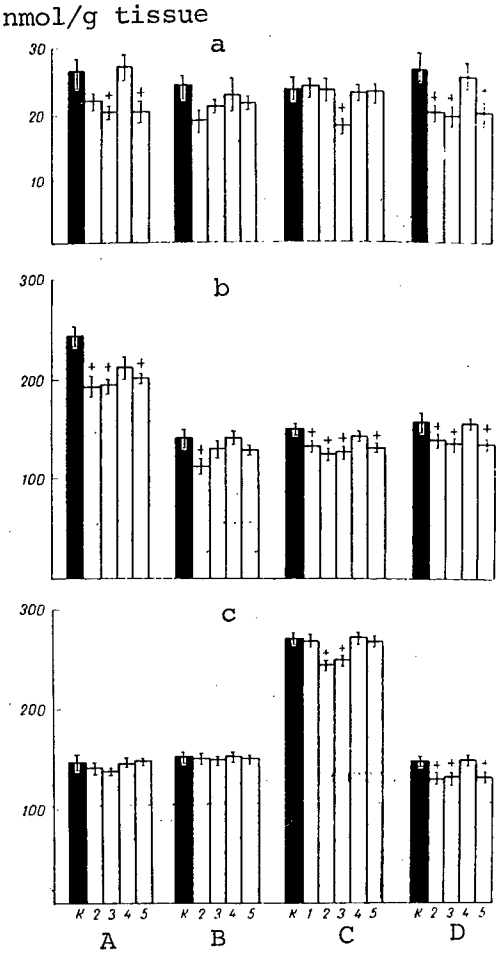
The studies were conducted on male Wistar rats weighing 200-250 g. Hypokinesia was produced by placing the animals in plastic box-cages [5]. After 15, 20, 30, 60 and 90 days of hypokinesia, we analyzed polyamine levels in the medulla oblongata, cerebellum, hypothalamic region and cerebral hemispheres by ion-exchange chromatography followed by electrophoresis [7]. Different parts of the brain were isolated following a special system [6]. The results were expressed in nanomoles per liter wet tissue. Statistical reliability of the data was assessed according to Student's t-test

Results and Discussion

Twenty-day hypokinesia was associated with decline in oblongata spermidine content and 30-day hypokinesia, with decline in putrescine and spermidine. On the 60th day of hypokinesia, polyamine levels did not differ from the control. On the 90th day there was again a decrease in concentrations of putrescine and spermidine (see Figure).

The cerebellum revealed only a decrease in spermidine contenton the 20th day of hypokinesia (see Figure).

In the hypothalamic region, 15-day hypokinesia led to decrease in concentration of spermidine; 20-day hypokinesia led to decline of spermidine and spermine levels; 30-day exposure led to decrease in all polyamines. On the 60th day of



Polyamine levels in different parts of the rat brain during hypokinesia

a) putrescine
b) spermidine
c) spermine
A) medulla oblongata
B) cerebellum
C) hypothalamic region
D) cerebral hemispheres
K) control
1-5) 15th, 20th, 30th, 60th and 90th days, respectively, of hypokinesia
+) reliable differences from the control

hypokinesia, polyamine concentrations did not differ from the control level, whereas on the 90th day there was another decline of spermidine level.

On the 20th, 30th and 90th days of hypokinesia, the cerebral hemispheres showed a significant decrease in concentrations of all polyamines, whereas on the 60th day their levels did not differ from the control (see Figure).

These findings indicate that different parts of the brain react differently to hypokinesia. The most marked changes in polyamine content in the direction of decrease in their concentrations are observed in the cerebral hemispheres, they are less marked in the hypothalamic region and medulla oblongata, and quite insignificant in the cerebellum. Apparently, the nerve centers of the animals' cerebellum adapt better to restricted motor activity, and there is less marked change in them with respect to intensity of biosynthetic processes in which polyamines are involved.

We must mention the undulant nature of the changes in polyamine concentrations in the tested parts of the brain in the course of 90-day hypokinesia: decline on the 20th-30th days (marked the most), normalization on the 60th day and another decline, though less significant, on the 90th day. The results of previous studies [1, 4], which indicated normalization of ACTH and epinephrine content of blood on the 60th day of hypokinesia, are consistent with these data. In all likelihood, the undulant nature of changes in polyamine levels indicates that there is periodic adaptation to constant stress.

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547.95:547.943]-06:612.89

REACTION OF SYMPATHECTOMIED RAT OPIOID SYSTEM TO IMMOBILIZATION STRESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 28 May 85) pp 87-90

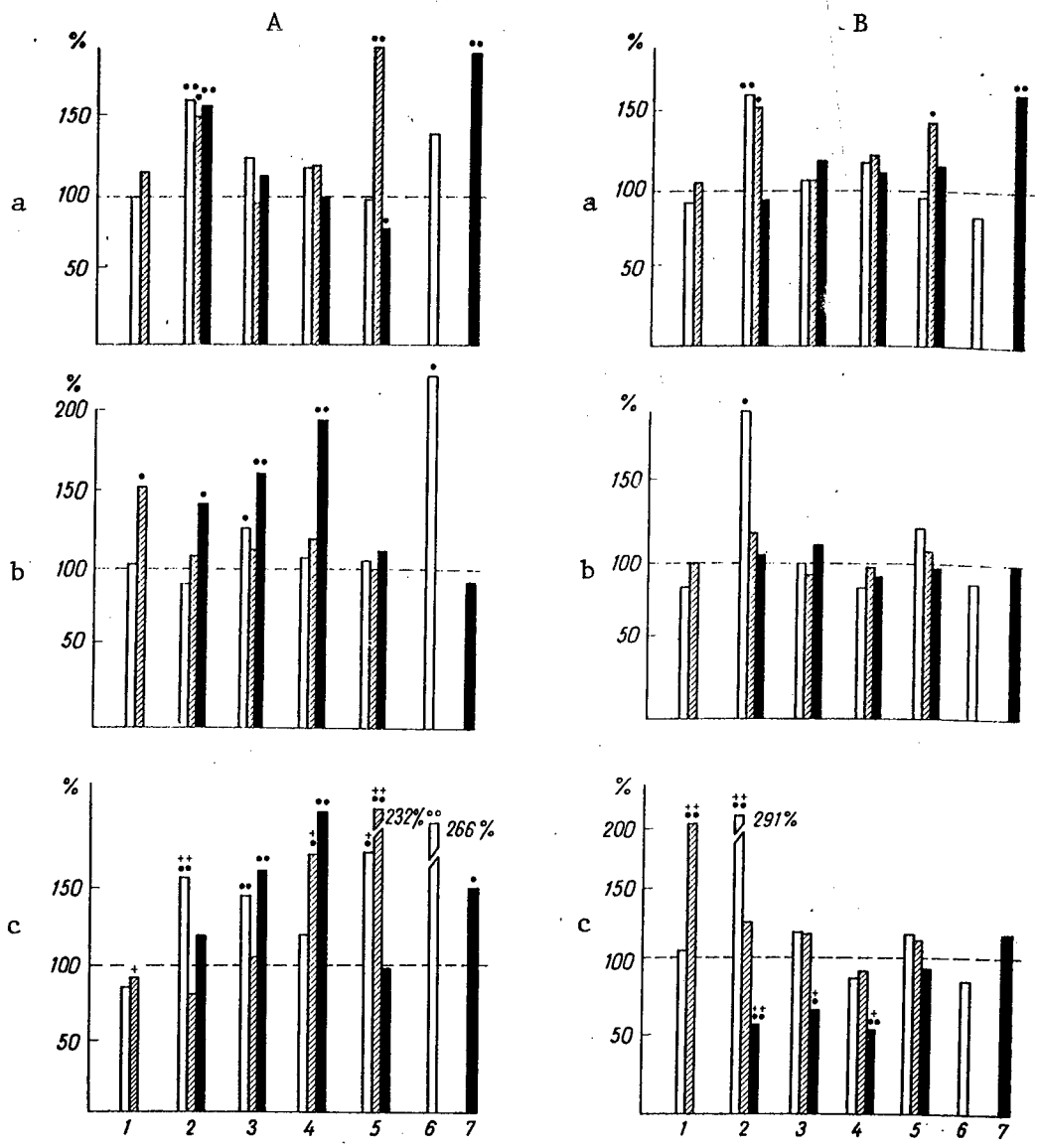
[Article by R. A. Tigranyan and O. P. Vakulina]

[Text] Catecholaminergic neurons of the brain form contacts with opioid neurons [13]. There are data in the literature to the effect that there are opiate peptides in sympathetic nerve endings [6]; however, little information is encountered about correlations between the catecholaminergic and opiate systems, and it is contradictory [1, 11]. It is assumed that opioids lower hyperactivity of noradrenergic neurons of the brain with exposure to stress [7]. On the other hand, catecholamines of the brain participate in expression of some effects induced by opioide peptides, for example, in control of retention [remebering] [2], or stimulation of prolactin secretion [12].

We studied here the reaction of the opiate system to immobilization, with change in functional state of the catecholaminergic system of the brain and peripheral adrenergic innervation.

Methods

This study was pursued on male Wistar rats weighing 220-260 g. Peripheral sympathectomy was performed by intraperitoneal injection of 6-oxidopamine (ODA), which elicits reversible degeneration of adrenergic terminals [8], in a dosage of 200 mg/kg in isotonic sodium chloride solution with 0.2% ascorbic acid. The experiment was performed on the 4th day after this injection. Destruction of catecholaminergic neuron endings of the brain was obtained by injection of 150 μg ODA in isotonic solution with 0.1% ascorbic acid into the third ventricle under stereotactic control; the experiment was conducted on the 6th day after administration of this agent. Control animals received intraperitoneal or intraventricular injections of isonotic solution with 0.2% or 0.1% ascorbic acid, respectively. To obtain immobilization, the animals were fixed on special tables for 150 min by the Selye method [9]. We analyzed levels of methionine enkephalin (ME), leucine enkephalin (LE) and β-endorphin (BE) in the hypothalamus, hypophysis, mesencephalon and medulla oblongata, enkephalins in the striatum, BE in blood plasma and ME in the adrenals. Enkephalin concentration in tissues and BE in blood and in the brain were assayed by the method of radioimmune analysis. Preparation of tissues for analysis has been described before [3]. Statistical reliability of the data was assessed according to Student's t criterion.



Opioid peptide content (% of control) after intraperitoneal (A) and intraventricular (B) injection of ODA

White bars--ME, striped--LE, black--BE. One dot indicates $P<0.05$, two indicate $P<0.01$, as compared to control rat parameters, + signs indicate the same as compared to sympathectomied animals.

a) isotonic solution + immobilization
b) ODA
c) ODA + immobilization
1) striatum
2) hypothalamus
3) mesencephalon
4) medulla oblongata
5) hypophysis
6) adrenals
7) blood plasma

Control values (in pmole/mg):
striatum 1.284±0.091 (ME), 0.469±0.035 (LE); hypothalamus 0.814±0.053 (ME), 0.319±0.025 (LE), 0.091±0.005 (BE): mesencephalon 0.287±0.091 (ME), 0.082±0.008 (LE), 0.0079±0.0005 (BE); medulla oblongata 0.225±0.019 (ME), 0.078±0.008 (LE), 0.0097±0.0012 (BE); hypophysis 0.727±0.074 (ME), 0.335±0.031 (LE), 3.92±0.21 (BE); adrenals 12.05±1.72 pg/mg (ME) blood 32.3±3.4 fmole/mℓ (BE)

Results and Discussion

Immobilization of animals after giving an injection of an isotonic solution led to marked rise of opioid levels in the hypothalamus, LE in the hypophysis, as well as increase in blood BE content, with concurrent decrease in the hypophysis (see Figure A,a), which is consistent with our data [3]. Sympathectomied animals (i.e., those given ODA), presented marked aggressiveness to one another. They showed increase in LE concentration in the striatum, ME in the midbrain and adrenals, as well as BE in the hypothalamus, midbrain and medulla oblongata (see Figure A,b). After immobilization of sympathectomied rats, opioid levels in the midbrain and medulla, as well as adrenals, remained elevated, enkephalin content of the hypophysis and ME in the hypothalamus increased, while LE concentration in the striatum and BE in the hypothalamus dropped to control levels; there was an increase in blood BE content without changes in its level in the hypophysis (see Figure A,c).

Thus, impairment of peripheral adrenergic innervation leads to changes in opioid peptide levels in the brain. There is also a change in effects of immobilization. In particular, we observed activation of opiate structures of the brain stem, which were not demonstrable in ordinary animals who were immobilized. There are data to the effect that blocking peripheral adrenergic transmission leads to excitation of central structures that control sympathetic nervous activity. It was shown that the blood-brain barrier is not permeable to ODA; however, intraperitoneal injection of ODA accelerates turnover of norepinephrine in the hypothalamus [5]. It can be assumed that elevation of opioid levels with injection of ODA (see Figure A,b) is the response of the opiate system to activation of catecholaminergic structures of the brain.

At present there is a rather definite idea about the routes of control of metabolism and secretion of catecholamines in the adrenals; however, there are very few such data concerning adrenal peptides [4, 14]. Adrenal opioid peptides are situated in chromaffin granules together with epinephrine, and they are secreted with catecholamines upon stimulation of splanchnic nerves [10, 14]. It is known that ODA does not impair adrenal innervation, and it elicits compensatory increase in their catecholamine content [8]. The increase in ME concentration in the adrenals (see Figure A,b), which we demonstrated, is indicative of changes in the same direction in catecholamines and enkephalins (along with their precursors) in the adrenals after chemical sympathectomy.

After intraventricular injection of isotonic solution, immobilization led to increase in enkephalin content in the hypothalamus, LE in the hypophysis and BE in blood (see Figure B,a). Unlike the results of the preceding series of experiments (see Figure A,a), we failed to demonstrate changes in endorphinergic systems of the hypothalamus and hypophysis, which is probably due to the surgical (stereotaxis) intervention. Injection of ODA was not associated with changes in opioid peptide content of the tested structures, with the exception of an increase in ME concentration in the hypothalamus (see Figure, B,b). After immobilization, sympathectomied animals showed a decline of BE level in the hypothalamus, mesencephalon and medulla oblongata, increase in LE content of the striatum and particularly in ME of the hypothalamus (see Figure B,c). Thus, in these rats the changes in opioid content with immobilization presented a different direction than ordinary animals (see Figure B,a), and this was particularly marked in the caudal parts of the brain.

Our findings warrant the assumption that, under normal conditions, catecholaminergic neurons of the brain have an insignificant effect on the opioid system, but in the presence of the stressor effect of hypokinesia, the nature of the response of the opiate system depends on the functional state of catecholaminergic neurons. At the same time, one should bear in mind the fact that the absence of changes in concentration of opioids after central sympathectomy, i.e., intraventricular injection of ODA (see Figure B,c) may reflect equilibrium between processes of synthesis and utilization of opioid peptides on a different level.

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RADIOSENSITIVITY OF ESCHERICHIA COLI FOLLOWING IRRADIATION IN A STATIONARY MAGNETIC FIELD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 12 Feb 85) pp 90-91

[Article by M. I. Minkova and T. P. Pantev (People's Republic of Bulgaria)]

[Text] There is change not only in general reactivity of an organism, but in different elements of the immune system under the effect of a stationary magnetic field (SMF) [1, 4, 5].

Saprophytic bacterial flora is present in the pressurized part of a craft. There is rather limited information about the effect of magnetic fields on microbial flora and its radiosensitivity. Our objective here was to test the effect of SMF on growth and radiosensitivity of E. coli B.

Methods

Experiments were performed with E. coli strain B. They were exposed to SMF between the poles of a permanent magnet at field intensity of $2.3 \cdot 10^5$ A/m. Radiation from ^{60}Co (8.17 Gy/min) was used to assess radiosensitivity.

We monitored reproduction of E. coli according to colony-forming activity after exposing a broth culture to SMF for 1, 3, 4, 5 and 24 h.

At first, we evaluated radiosensitivity with use of 50-600 Gy of a suspension of E. coli in saline exposed to SMF for 24, 48 and 72 h at room temperature. The irradiated specimens were reinoculated on agar, incubated at 37°C for 48 h, and then we determined cell survival rate. In anotherexperimental protocol, cells were exposed to SMF after irradiation.

Results and Discussion

SMF affects growth of E. coli (Figure 1). In the opinion of some authors, SMF has a stimulating effect on growth of microorganisms [3]. Other authors believe that it elicits a bacteriostatic and even bactericidal effect [6, 8]. On this basis, it can be concluded that the effect of SMF depends chiefly on its direction, duration of exposure to it, as well as some additional conditions, for example, temperature, pH, etc.

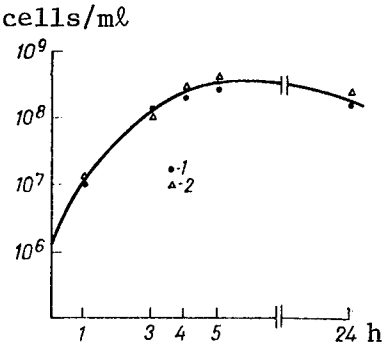

Figure 1.
Effect of SMF on reproductive capacity of E. coli B
1) cells that grew under normal conditions
2) cells that grew in SMF

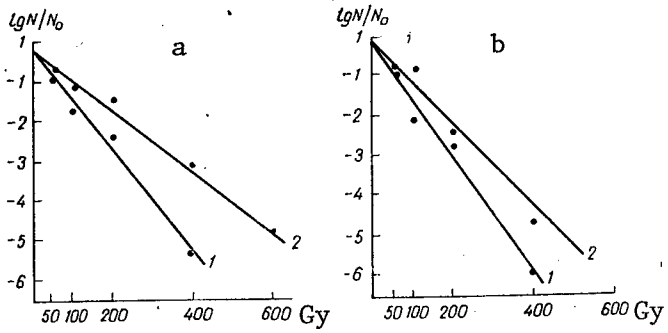

Figure 2.
Changes in radiosensitivity of E. coli B exposed to SMF for 24 a (a) and 48 h (b) before exposure to γ-radiation
Here and in Figure 3: 1) γ-radiation
2) SMF + γ-radiation

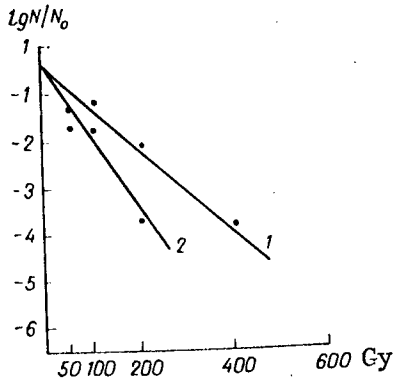

Figure 3.
Change in radiosensitivity of E. coli B exposed to SMF for 72 h before irradiation

Exposure of bacterial cells to SMF alters significantly their radiosensitivity. A comparison of dose-effect curves for a control suspension and one exposed to SMF for 24 h shows that there is considerable enhancement of radiation resistance in the latter case (Figure 2). A dosage of 600 R, which is absolutely lethal for intact cells, does not lower colony-forming capacity of cells exposed to SMF alone.

Figure 2b illustrates the effect of 2-day exposure of bacterial cells on their radiosensitivity. In this case too, the effect of SMF consists of decline in radiosensitivity of E. coli.

However, exposure of the bacterial suspension to SMF for 72 h elicits the opposite effect, i.e., distinct increase in radiosensivity of the strain (Figure 3). With a radiation dose of 200 Gy, when there is maximum expression of damage to exposed cells, the difference in colony-forming capacity between control and experimental samples constitutes almost a factor of 10^2.

Exposure of the bacterial suspension to SMF following γ-irradiation in the same doses does not affect postradiation survival of the strain. There is the same extent of cell deaths among both control microorganisms and those exposed to SMF for 24, 48 and 72 h.

Thus, the dose modification factors (DMF) with exposure to SMF before irradiation constituted 1.58, 1.37 and 0.52 ($P<0.05$), respectively, and in the case of exposure to SMF after irradiation, they were 0.92, 0.97 and 1.10 ($P>0.05$).

Combined exposure to SMF and ionizing radiation leads to distinct quantitative changes in different directions, with regard to inactivation of E. coli strain B. The nature of the dose-effect function did not change under the effect of SMF.

Our findings indicate that, under certain conditions, SMF can elicit a radioprotective effect. The degree of this effect is a function of duration of exposure. DMF levels indicate that the protective effect of SMF diminishes with increase in duration of exposure, after which there is increase in radiosensitivity.

There are only sparse data in the literature concerning change in radiosensitivity [2] and antibiotic resistance [3] of E. coli under the influence of SMF. No doubt, it is of some interest to expand investigations in this direction.

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RADIOPROTECTIVE EFFECT OF INSOLUBLE POLYANION ON LONG-TERM EXPOSURE TO GAMMA RADIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 12 Feb 85) pp 92-93

[Article by M. I. Minkova, T. P. Pantev, M. Talash and L. Batkay (People's Republic of Bulgaria)]

[Text] With increase in duration of spaceflights, the probability of complication of the radiation situation increases. It becomes necessary to provide radioprotection by means of pharmacochemical agents. The protracted and nonuniform nature of irradiation under spaceflight conditions limits the use of known radioprotective agents. Researchers are concentrating their efforts on the study of agents that are effective when used for therapeutic or preventive purposes.

Previously conducted investigations established that insoluble polyanion (copolymer of maleic and methacrylic acids) has a radioprotective effect in the case of both preventive and therapeutic administration during total-body single exposure to radiation [1-4].

Our objective here was to test the protective properties of polyanion in the case of long-term exposure to γ-radiation.

Methods

We used line H male mice with average wieght of 25 g in our experiments. They were exposed to radiation from a ^{137}Cs source at a dose rate of 3.1 μA/kg (0.74 R/min) to a cumulative dose of 5 and 10 Gy. Polyanion (Patent No 169981 of the Hungarian People's Republic) was injected once intraperitoneally in a dosage of 4 mg/kg 1 or 3 h after irradiation. We evaluated the effect of this agent on the 3d postradiation day according to weight, total and specific cellularity of the spleen, number of myelokaryocytes in the femur and total leukocyte count in peripheral blood. The animals were sacrificed under ether anesthesia.

Averaged values of tested parameters were obtained for 10 mice from each group.

Effect on mice of insoluble polyanion with long-term exposure to cesium γ-rays (3.1 μA/kg, dosage 5 and 10 Gy)

Parameter	Radiation dose, Gy 5		
	control	polyanion (4 mg/kg)	
	–	after 1 h	after 3 h
Spleen weight, mg	61,40±2,78	61,75±3,65	112,18±5,15*
Total cellularity of spleen, 10^6/organ	92,48±4,03	65,82±1,03*	125,54±5,68*
Specific cellularity of spleen, 10^6/mg tissue	1,31±0,02*	1,06±0,04*	1,31±0,03*
Total myelokaryocytes, 10^6/femur	9,12±0,26	6,50±0,42*	11,00±0,35*
Blood leukocytes	5300±203	5700±292	3800±230*

Parameter	Radiation dose, Gy 10		
	control	polyanion (4 mg/kg)	
	–	after 1 h	after 3 h
Spleen weight, mg	46,00±3,53	38,66±4,20	42,66±0,50
Total cellularity of spleen, 10^6/organ	38,37±3,22	50,37±2,85*	50,50±0,44*
Specific cellularity of spleen, 10^6/mg tissue	0,76±0,02*	0,92±0,06*	1,10±0,02*
Total myelokaryocytes, 10^6/femur	3,29±0,23	3,38±0,14	6,10±0,48*
Blood leukocytes	1600±168	2100±106*	1900±106

* $P < 0,05$.

Results and Discussion

The table lists the results of the therapeutic effect of polyanion on lesions to the hemopoietic system of mice exposed to long-term radiation.

No protective effect on the spleen and bone marrow was observed when the agent was given 1 h after exposure to a total radiation dose of 5 Gy. The changes in different directions, which are reliable, cannot be interpreted as the possible effect of polyanion on radiation damage to hemopoiesis.

Administration of the agent 3 h after delivery of the same dose of radiation has a beneficial effect. Weight and total cellularity of the spleen were about 82 and 35% higher, respectively, in injected animals than the control. The number of bone marrow cells was also 20% higher.

The agent had an analogous effect on animals exposed to a total dose of 10 Gy (see Table). Injection of the agent 1 h after irradiation leads to increase (by about 30%) in number of spleen karyocytes and leukocytosis of peripheral blood. However, spleen weight and cellularity of bone marrow do not change. At the same time, polyanion has a more marked beneficial effect on radiation

damage to hemopoietic organs when it is injected 3 h after irradiation. In this case, total and specific cellularity of the spleen of experimental animals was about 30 and 50% higher, respectivley, and the number of myelokaryocytes 85% higher.

On the basis of these data, it can be concluded that, in the case of long-term exposure to radiation in a dosage of 5-10 Gy, administration of this agent 1 and 3 h after exposure has some positive effect on the spleen and bone marrow, which is manifested by attenuation of early radiation damage to hemopoietic tissues. The effect of polyanion is more distinctly demonstrable when it is given 3 h after irradiation.

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EMETIC EFFECT OF ENKEPHALINS, BETA-ENDORPHIN AND MORPHINE ON CATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (manuscript received 31 Jan 86) pp 93-95

[Article by V. V. Yasnetsov, Yu. V. Drozd, V. S. Shashkov and Yu. I. Ryumin]

[Text] The endogenous peptide that has morphine-like properites, methionine enkephalin, elicits vomiting in cats when injected intraventricularly in a dosage of 1-2 mg [1, 4-6]. It is believed that the emetic effect of endogenous opioid peptides is attributable to their influence on opiate receptors of the chemoreceptor triggering zone of the vomiting center, the presence of which has been demonstrated by several authors [3, 4, 7]. However, no special studies have been conducted to determine the distinctions of the emetic effect of various representatives of endogenous morphine-like substances.

Our report deals with a comparative study of the emetic effects of enkephalins, β-endorphin and morphine on cats, with due consideration of their role in the pathogenesis of motion sickness [2].

Methods

Experiments were performed on 15 nonanesthetized male cats weighing 2.3-3.4 kg whose behavior was unrestricted. A cannula was implanted under anesthesia (sodium pentobarbital, 30-40 mg/kg intraperitoneally) in the cavity of the 4th ventricle of the brain according to the following atlas coordinates [9]: P = 11, L = 0, H = -4.5, 3-5 days prior to the experiment. The position of the cannula in the fourth ventricle was then verified using Evans' dye upon autopsy. In the course of the experiments, we recorded the ECG and respiration on a polygraph, then from these data we determined the heart rate (HR) and respiration rate (RR).

Morphine, enkephalins and β-endorphin (the opioid peptides were synthesized in the laboratory for peptide synthesis of the All-Union Cardiological Research Center, USSR Academy of Medical Sciences)* in doses of 10-300 μg were dissolved in sterile isotonic sodium chloride solution and injected into the fourth ventricle with a microsyringe in a volume of 50-100 μl. Naloxone, which is

*We wish to express our gratitude to Prof M. I. Titov for kindly furnishing these agents.

Effect of opioid peptides and morphine on HR and RR of cats during and after emesis (M±m)

Agent (dosage, μg)	Number of cats	LP, s	BL	1 min after injection	During emesis (2-6min)	Time after vomiting, min					
						1	3	5	10	15	20	25
HR per min												
Morphine(10-100)	7	214±41	161±14	154±10	144±11	154±8	134±10	126±10	124±8*	123±8*	123±8*	122±7*
ME (10-100)	5	144±35	173±12	164±13	158±15	163±14	161±17	152±13	168±14	158±13	177±18	182±22
LE (10-100)	5	125±29	154±5	160±2	174±4**	155±2	133±9	134±16	104±9***	117±14*	141±10	111±6****
BE (10-100)	5	181±47	165±12	160±2	155±9	169±15	147±10	151±14	148±11	151±13	155±13	162±15
RR per min												
Morphine(10-100)	7	214±41	48±6	54±7	46±3	44±6	51±6	48±6	47±6	45±2	45±7	46±3
ME (10-100)	5	144±35	33±3	34±4	46±8	41±9	53±13	36±6	38±6	40±7	31±4	34±6
LE (10-100)	5	125±29	45±8	45±7	64±26	52±14	68±28	46±14	46±14	43±12	63±17	48±14
BE (10-100)	5	181±47	35±8	32±6	31±6	31±6	46±18	46±20	36±5	33±4	35±4	33±4

Key: LP) latency period of emetic reaction ME) methionine enkephalin LE) leucine enkephalin
BE) beta-endorphin BL) baseline

*P<0.05, as compared to baseline (Student's criterion) **P<0.02 ***P<0.002
****P<0.001

a specific opiate and opioid antagonist, was used to block opiate receptors.

Results and Discussion

Opioid peptides and morphine, when injected in the fourth ventricle of the brain, induced vomiting in all animals, once or many times, depending on the dosage (no emetic effect was observed after control injections of 100 μl sterile isotonic sodium chloride solution). The table lists data on the effect of the agents on HR and RR of cats during and after vomiting, as well as latency periods of the emetic reaction for each of the products indicated. This table shows that enkephalins, β-endorphins and morphine, in doses of 10-100 μg, do not alter RR of the animals. Unlike the RR, the HR turned out to be a more informative parameter. Thus, the emetic effect of leu-enkephalin was associated with tachycardia, which was followed by bradycardia. Morphine had a somewhat different effect: both during and after vomiting there was slowing of HR. Methenkephalin and β-endorphin did not elicit statistically reliable changes in HR (see Table).

The specific agent that blocks opiate receptors, naloxone, prevented the emetic effect entirely in 7 out of 8 cases when injected in the fourth ventricle in doses of 15-105 μg 1-2 min before administration of the opioid peptides and morphine (in 1 test, 100 μg naloxone did not block the emetic effect of the same dose of β-endorphin). With use of naloxone, no statistically reliable changes in HR were demonstrable after administration of morphine and leu-enkephalin. These data indicate that the emetic reaction induced by endogenous opioids and morphine is attributable to stimulation of opiate receptors of the chemoreceptive trigger zone of the vomiting center. It must be noted that a high dose of naloxone (100 μg) elicited vomiting in one of the experiments. An

analogous effect of this agent on dogs was previously discovered by Bhargava et al. [4]. These facts warrant the assumption that naloxone in large doses either has agonistic activity or begins to display "nonspecific" elements, i.e., it not only blocks opiate receptors but also affects, for example, dopaminergic and GABA-ergic structures of the brain, as indicated in [8].

Thus, the results of this investigation revealed that different representatives of endogneous opioid peptides have emetic properties: by interacting with opiate receptors in the chemoreceptive trigger zone of the vomiting center, they can induce the vomiting reaction in animals. This is important to understanding the central mechanisms of onset of emesis of diverse genesis, including motion sickness.

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BOOK REVIEW

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NEW BOOK DEALS WITH NONSPECIFIC MECHANISMS OF HUMAN ADAPTATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 20, No 6, Nov-Dec 86 (signed to press 31 Oct 86) pp 95-96

[Review by V. I. Kopanev and V. N. Bortnovskiy of book, "Nespetsificheskiye mekhanizmy adaptatsii cheloveka" [Nonspecific Mechanisms of Human Adaptation] by I. A. Sapov and V. S. Novikov, Nauka Publishing House, Leningrad, 1984, 146 pages]

[Text] The monograph by I. A. Sapov and V. S. Novikov is the first basic work summarizing the results of the authors' many years of investigation of the role of protective systems in physiological mechanisms of adaptation. In the book, there is in-depth analysis of data on resistance and reactivity of the human body when exposed to various extreme factors; it discusses the patterns and mechanisms of protective system dysfunctions from the general biological point of view; it demonstrates that nonspecific adaptive responses reflect the most general principles of genesis of adaptation and can serve as a criterion of its effectiveness. The vast material obtained from full-scale studies enabled the authors to establish the phenomenology of functional changes in defense systems under the effect of extreme factors, to define the role of nonspecific elements of chronophysiological adaptation and develop theory of nonspecific mechanisms of adaptation.

The book consists of an introduction, four chapters and conclusion.

The introduction validates the timeliness of the adaptation problem, justifies the need for investigation of cellular mechanisms of homeostasis, formulates theses on nonspecific mechanisms of adaptation as a new scientific and clinical direction within the framework of the "Human Adaptation" program.

In Chapter 1, the authors acquaint the reader with the range of basic scientific and applied problems of adaptation, and they dwell in detail on homeostatic mechanisms of adaptagenesis. In this chapter, a large space is devoted to information about the state of cellular and humoral factors of nonspecific defense under extreme environmental conditions. Data are submitted about the main patterns of adaptive changes and causes of weakening of nonspecific defense of the body in polar regions; there is detailed discussion of the etiopathogenesis of hematological changes and mechanisms of dysfunctions of defense systems. The investigations pursued by the authors can serve as the basis for dividing into periods the process of adaptation to new climate and geographic

conditions; they expand considerably conceptions of physiological reserves of the body and condition of healthy individuals as a whole. As they develop conceptions of significance of nonspecific elements in physiological mechanisms of adaptation, the authors submit unique data concerning stability of adaptive changes in the course of human readaptation to high latitudes. It is shown that changes in defense functions of the body in the course of repeated adaptation of man to polar conditions do not essentially differ from the dynamics of adaptagenesis in nonadapted individuals, which is indicative of instability of adaptive changes when people move in a latitudinal direction.

Chapter 2 submits original data from studies of the effect of physical conditioning on nonspecific resistance of man. It is shown that wisely planned exercise accelerates development of stable forms of adaptation; it is an effective means of enhancing the defense potential of the body and preventing various diseases.

Chapter 3 is of great interest; it deals with biorhythmological organization of defense functions. As we know, this is a rather relevant question to aerospace medicine because of the need for equilibrated rhythms of biological processes with the rhythms of the numerous factors to which man is exposed under such conditions. Changes in environmental and social factors have a substantial effect on dynamics of biorhythms and could cause impairment of the usual amplitude and phase correlations in synchronized systems of the body as a whole. In this chapter, the authors do not limit themselves to making a statement about circadian and circannual rhythms of defense systems; rather, they disclose their order and mutual determination in the dynamics of the adaptation process. For the first time they demonstrated that the changes in biorhythmological organization of defense systems, which occur in the course of chronophysiological adaptation, have a direct effect on the rate of formation of the biological timing of circadian and circannual rhythms. A practical evaluation of this results makes it possible to conclude that long-term desynchronization of circadian rhythms retards the adaptation process and could become the primary cause of development of various desynchronoses.

Chapter 4 is concerned with the problem of adaptation and resistance of seamen. The extensive material in this monograph pertaining to studies of the state of defense functions in naval specialists expands significantly conceptions about the possible optimization of physiological and hygienic sailing conditions and prevention of deadaptation changes in naval personnel. It was shown that the most important elements of medical support of long-term voyages are: implementation of monitoring of the adaptation (readaptation) process; establishment of quantitative criteria of adaptation and deadaptation; validation of the ways, methods and means of enhancing nonspecific resistance and retaining work capacity of ship specialists. The section dealing with questions of regulation of cellular mechanisms of homeostasis in the presence of extreme factors is of exceptional importance.

In the conclusion of this book, there is a summary of the basic theses of theory of nonspecific mechanisms of adaptation. Viewing resistance as the result of adaptive reactions aimed at maintaining homeostasis, the authors demonstrated convincingly that it is possible to predict the course of the adaptation process and detect prenosological states according to the extent of tension of nonspecific mechanisms of adaptation. It should be noted that the

authors' interpretation of nonspecific mechanisms, patterns and criteria of extent of tension of adaptation processes is already being confirmed by practice, as indicated by the successful use of preventive measures developed on this basis.

The book being reviewed is the first work that discusses extensively one of the most important and least studied problems of medicine and biology--nonspecific mechanisms of adaptation. Its publication is the basis for subsequent theoretical generalizations in different branches of physiology and medicine. The important qualities of the monograph include a clear style of presentation, good illustrations, modern terminology, in-depth analysis of the literature, validated methodological approaches to predicting individual adaptation of man. The importance of the problem, depth and fullness of consideration, as well as high competence of the authors, places this monography in the ranks of basic works in Soviet physiology. We believe that the monograph will get a warm response from physiologists, biologists, ecologists, and physicians concerned with adaptation problems.

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